BONE TUMORS

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General Aspects and an Analysis of 2,276 Cases

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Preface

MANY OF THE MAJOR ADVANCES in present-day understanding of neoplastic and nonneoplastic diseases of bone have been made in the last two decades. In the light of current concepts, I have reviewed systematically all the bone tumors in the files of the Mayo Clinic prior to 1956. I began this review 9 years ago, and have had the help of several of my colleagues who have collaborated in the study of various facets of the over-all problem, as is indicated in the bibliography. The study has embraced more than 2,000 consecutive, unselected bone tumors. Correlation of the clinical features with the gross and microscopic features has been possible because both the case records and the gross and microscopic specimens have been available for study. Complete follow-up studies were available in almost 100 per cent of cases largely because of the work of Dr. Henry W. Meyerding, emeritus member, Section of Orthopedic Surgery, Mayo Clinic, and emeritus professor of orthopedic surgery, Mayo Foundation, Graduate School, University of Minnesota, whose active interest in bone tumors covered a span of nearly 40 years.

Data derived from this study were first presented in the form of an exhibit at the annual meeting of the American Medical Association held in Chicago in June, 1956. Information on skeletal localization and on age and sex distribution, as well as roentgenograms, photomicrographs, and illustrative moulages of gross specimens, was included. As a result of this exhibit, a number of orthopedic surgeons, roentgenologists and pathologists asked me to make the accumulated data available for reference. This I have attempted to do in this small volume, which is an amplification of the material presented in the exhibit.

Because proper understanding of the neoplasms of bone demands correlation of their roentgenologic, gross and microscopic features, these features are liberally illustrated. Textual material has been kept to a minimum and theoretical considerations have been almost completely avoided. The bibliography has been restricted to a few of the pertinent contributions on each subject.

In the final chapter I have discussed briefly several nonneoplastic diseases of bone because they are among those that may be confused clinically and roentgenologically with neoplasms of bone. Odontogenic tumors, because of the special problems they pose, have not been included in the series.

I am indebted to Dr. David G. Pugh, of the Section of Roentgenology of the Mayo Clinic, for his review of the illustrative roentgenograms and of the comments on the roentgenologic features of bone tumors. From Dr. Emer W. Johnson, Jr., and Dr. William H. Bickel of the Section of Orthopedic Surgery, I have received invaluable aid in preparation of the comments on therapy. I am also indebted to the entire staff of the Section of Orthopedic Surgery for their co-operation in this project. To Dr. Carl M. Gambill, of the Section of Publications, and to the Section of Photography, the Section of Biometry and Medical Statistics and the Art Studio I am grateful for their contributions to this book. Dr. Arthur H. Bulbulian, of the Mayo Foundation Museum of Hygiene and Medicine, did much of the work on the original exhibit of bone tumors.

D. C. D.

Contents

BONE TUMORS

Chapter 1

Introduction and Scope of Study

THE TABULATED STATISTICS included in this book are those of an unselected series of bone tumors except for the following factors. A case was included only if a complete surgical specimen or adequate material for biopsy had been obtained. No case was included in which histologic verification of the diagnosis according to modern pathologic concepts was impossible. The pathologic features were currently reviewed in every case. The patients had all come to the Mayo Clinic for care, thus introducing a possible selection factor of questionable significance.

Accurate analysis of many of these tumors would have been impossible but for the fact that the entire gross specimen, preserved in 10 per cent formalin solution, was available for review in practically every case. A sufficient number of new microscopic sections were made to assure that the various gross features of each lesion could be studied histologically. Such new sections were essential for the correct interpretation of certain lesions. In the average aneurysmal bone cyst, for example, the microscopic section on file was often from a nonspecific solid portion and it was necessary to imbed the curetted fragments from the specimen bottle in paraffin to obtain a preparation that reconstructed the true pathologic appearance to a degree sufficient for correct diagnosis.

Roentgenograms or the interpretations of them were correlated with the gross and histopathologic features. Although x ray shadows do not supplant microscopic sections in final diagnosis, they frequently afford practically conclusive evidence of the malignant or benign nature of bony lesions and often indicate the histologic type. The roentgenogram may be considered part of the gross pathologic picture, delimiting as it does the part of the bone affected and, in large measure, the extent of the disease. The pathologist responsible for the diagnosis of osseous lesions handicaps himself immeasurably if he ignores their roentgenographic features. These features provide a useful guide for proper biopsy. Anyone can determine, for instance, the inadequacy of an inconclusive needle biopsy specimen or a gram of necrotic tissue excised from a tumor that gives the roentgenologic appearance of having destroyed half of a femur.

In the case of most bone tumors the patient's local symptoms and the results of physical examination are relatively nonspecific. The usual symptoms, pain or swelling or both of these, serve mainly as a guide to the correct site for roentgenographic studies and for biopsy. Accordingly, clinical features of bone tumors have been relegated to a relatively minor place in the discussions to follow. Occasionally, however, as with osteoid osteoma that may give referred pain at a site well away from the lesion, clinical judgment is all important. In some patients, systemic signs and symptoms provide helpful evidence for a specific diagnosis but more often these signs and symptoms are basically nonspecific.

In the interest of brevity a somewhat dogmatic stand will be presented in the chapters to follow. This will be based on the study of Mayo Clinic cases and a review of the literature. When significant differences of opinion exist, these will be indicated in the text or in the bibliography.

Classification

The classification used in this book (table 1) is similar to that advocated by Lichtenstein One of the significant differences is that there has been little attempt to draw a relationship between the benign and the malignant tumors because so few of the latter take origin from the former The classification is based on the cytology or the recognizable products of the cells of the neoplasms. In most instances, the tumors apparently arise from the type of tissue they produce but such an assumption cannot be proved correct. For example most chondrosarcomas begin in portions of bone that normally contain no obvious benign cartilaginous zones. In any event, basing a classification on what is actually seen histologically allows reduplication of results on subsequent analysis.

Myxomas and myxosarcomas practically never occur in any portion of the skeleton except the jawbones. Accordingly they have been omitted from the general classification in table 1 Chondrosarcomas and chondromyxoid fibromas often bear a superficial resemblance to myxomas. Possibly the myxoid tumors seen occasionally in the mandible and maxilla are of odontogenic derivation.

Hematopoietic Tumors

The hematopoietic tumors, numbering 633 cases, were the most prevalent tumors of bone in the files of the Mayo Clinic. These included 563 cases of myeloma. Malignant lymphomas of bone, which ordinarily contain a predominance of reticulum cells and are generally referred to as reticulum cell sarcomas contributed 70 cases Leukemic tumor nodules in bone, although they are commonly found in the terminal phases of leukemia, rarely masquerade clinically as primary malignant disease of bone, and none were encountered in this surgical series.

Chondrogenic Tumors

The second largest group consisted of chondrogenic tumors. The tumors in this group were placed there because their histologic appearance proved or suggested a relationship to hyaline cartilage. Slightly more than one fourth of the total series were in this group and the osteochondromas (osteocartilaginous exostoses) constituted nearly half of the chondrogenic group Osteochondromas result from growth of their cartilaginous caps, making them basically chondrogenic. Chondromas whether they be centrally or subperiosteally located, are tumors of hyaline cartilage which may show variable amounts of calcification and ossification within their substance. Benign chondroblastomas have been separated from the "waste basket" of giant cell tumors of bone because their proliferating cells produce foci of a matrix substance quite like that of hyaline cartilage. Although chondromyxoid fibromas have a variegated histologic appearance, large or small zones ordinarily bear a striking resemblance to hyaline cartilage. Both primary and secondary chondrosarcomas are obviously related to the chondrogenic neoplasms

Osteogenic Tumors

In the osteogenic group of tumors the 490 sarcomas dominated the picture. For a tumor to qualify for this group the malignant neoplastic cells of the given tumor must, in at least some portions, produce recognizable osteoid substance With this basic qualification the osteogenic sarcomas logically fall into three classes, namely osteoblastic, chondroblastic and fibroblastic, depending upon the dominant histologic picture The basic biologic behavior of these three tumor subtypes, however is quite similar as will be shown in the chapter devoted to osteogenic sarcoma

The clinically indolent and pathologically slowly progressing low grade tumors that have become generally known as parosteal osteogenic sarcomas have been placed in a separate subdivision. The rarity of parosteal osteogenic sarcoma has produced some confusion regarding the authenticity of the entity

In the Mayo Clinic files there are 57 examples of ordinary osteoid osteoma. Without delving into the controversy as to whether this lesion represents a true neoplasm or some peculiar reaction in bone, we have arbitrarily classed it with the bone tumors The 17 tumors that we have called "giant osteoid osteomas" represent an unusually controversial group of cases. Lesions of this type have been called "osteogenic fibromas," "ossifying fibromas" and more recently osteoblastomas." We have employed the term giant osteoid osteoma because this tumor bears such a close histologic resemblance to ordinary osteoid osteoma. The prefix giant is meant to indicate a different biologic behavior since tumors of this type do not share the strictly limited growth potential of the average osteoid osteoma although they are generally just as curable.

Tumors of Unknown Origin

The commonest tumor of unknown origin was Ewing's tumor constituting 141 cases. Benign giant cell tumor with 109 cases, was almost as prevalent. The giant cells of the benign giant cell tumor appear to arise from the stromal cells the exact origin of which is unknown. It has been suggested that they arise from undifferentiated mesenchymal cells of bone. It is impossible to substantiate the diagnosis of malignant giant cell tumor unless one can demonstrate typical zones of benign giant cell tumor in the current or previous tissue from the same case. We had only 11 bona fide malignant giant cell tumors. The epithelial tumor, adamantinoma of long bone, is of unknown origin and only five examples were present in this series.

Fibrogenic Tumors

The pathologic entity called fibroma of bone," although quite likely not neoplastic, has been included among the bone tumors because of common usage. The files contained 35 examples. Only 58 pure fibrosarcomas of bone were encountered. It should be stressed, however that multiple sections of all of the tumors were made and osteoid production in any portion of a predominantly fibroblastic tumor relegated it to the osteogenic sarcoma group.

Notochordal Tumors

This series included 80 chordomas. Although this tumor rarely metastasizes, it produces death of its host by local recurrence and extension and hence it has been placed in the category of malignant tumors.

Tumors of Vascular Origin

Although the angiomatous tumors are relatively commonly manifested in roentgenograms, less than 1 per cent of the histologically verified neoplasms in this series were in this group. Thirteen of these were hemangiomas most of which involved bones of the skull Two were hemangiopericytomas, and three were obviously malignant blood vascular tumors.

Lipogenic Tumors

Two lipomas of bone were found. In no case did it seem possible to substantiate the unequivocal diagnosis of liposarcoma The occasional tumor with multinucleated malignant cells, possessing foamy cytoplasm and suggesting the possibility of an origin from adipose connective tissue was classed with the osteogenic sar

comas. This decision was based on the observation that a similar histologic appearance was present in other tumors which contained zones of obvious osteogenic sarcoma.

Neurogenic Tumors

The single neurilemmoma of bone in the present series involved the mandible. No malignant neurogenic tumors originating in bone were recognized.

Unclassified Tumors

A few tumors had to be discarded from the total series because there was insufficient tissue for accurate classification. Another group, constituting approximately 1 per cent of the total, did not fall into a niche in the classification. These neoplasms form a heterogeneous group that, for the time being, must be called "unclassified."

Skeletal and Age Distribution

Table 3 shows the skeletal distribution of the various types of tumors. It affords the reader a convenient guide for comparative incidence whether he is interested in a specific neoplasm or an affected bone. The knowledge that certain bones are practically immune to some tumors and have a marked predilection to be the site of development of other neoplasms often assists one in arriving at a correct diagnosis. It is noteworthy, for instance, that only three of 490 osteogenic sarcomas affected bones of the hands and wrists and that all 13 tumors of the sternum were malignant.

Some tumors have a decided predilection for patients in certain age groups. Knowledge of this predilection is often useful in arriving at a presumptive preoperative diagnosis. The succeeding chapters indicate, with bar graphs, the age distribution for each neoplasm. For specific figures the reader is referred to table 2.

TABLE 2

Distribution of Tumors by Histologic Type and by Age of Patients

Histologic type	*Age Distribution by Decades*									*Total*
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	
					Benign					
Hematopoietic										None
Chondrogenic										
Osteochondroma	30	103	58	36	22	13	9	1		272
Chondroma	5	19	21	19	14	16	2	3		99
Chondroblastoma	1	9	2	1	1	3				17
Chondromyxoid fibroma	2	2	7	1		1				13
Osteogenic										
Osteoid osteoma	8	25	15	6	1	1	1			57
Giant osteoid osteoma	2	5	6	1	1	1	1			17
Unknown origin										
Giant cell tumor		11	41	31	17	6	3			109
Fibrogenic										
Fibroma	4	14	8	3	2	4				35
Notochordal										None
Vascular										
Hemangioma	1			1	8	2	1			13
Hemangiopericytoma					1			1		2
Lipogenic										
Lipoma				1	1					2
Neurogenic										
Neurilemmoma							1			1
Total benign	53	188	158	100	68	47	18	5		637

TABLE 2

DISTRIBUTION OF TUMORS BY HISTOLOGIC TYPE AND BY AGE OF PATIENTS

Histologic type	*Age Distribution by Decades*									*Total*
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	
Benign										
Hematopoietic										None
Chondrogenic										
Osteochondroma	30	103	58	36	22	13	9	1		272
Chondroma	5	19	21	19	14	16	2	3		99
Chondroblastoma	1	9	2	1	1	3				17
Chondromyxoid fibroma	2	2	7	1		1				13
Osteogenic										
Osteoid osteoma	8	25	15	6	1	1	1			57
Giant osteoid osteoma	2	5	6	1	1	1	1			17
Unknown origin										
Giant cell tumor		11	41	31	17	6	3			109
Fibrogenic										
Fibroma	4	14	8	3	2	4				35
Notochordal										None
Vascular										
Hemangioma	1			1	8	2	1			13
Hemangiopericytoma					1			1		2
Lipogenic										
Lipoma				1	1					2
Neurogenic										
Neurilemmoma							1			1
Total benign	53	188	158	100	68	47	18	5		637

TABLE 3

LOCALIZATION DATA ON 1,853 BONE TUMORS

(Exclusive of 4[illegible]3 Cases of Multiple Myeloma)

	Femur	*Tibia*	*Innominate*	*Humerus*	*Vertebra*	*Ribs*	*Sacrum*	*Hand*	*Scapula*
Osteochondroma	79	37	26	52	7	9	1	7	21
Chondroma	12	1	3	6	4	3		56	3
Chondroblastoma	7		4	3		1			2
Chondromyxoid fibroma	2	6	2						
Osteoid osteoma	23	15	3	4	1			1	2
Giant osteoid osteoma	2	4		1	7		1		
Giant cell tumor	37	25	5	6		1	11		
Fibroma	12	14	2	3		2			
Hemangioma			1	1	2				
Hemangiopericytoma									
Lipoma									
Neurilemmoma									
Total benign	174	102	46	76	21	16	13	64	29
Myeloma	5	4	20	6	47	17	8		2
Reticulum cell sarcoma	18	9	6	8	6	4			5
Primary chondrosarcoma	38	9	48	8	13	46	3	1	11
Secondary chondrosarcoma	1		10	3		1	1		2
Osteogenic sarcoma	214	94	40	38	6	10	2	3	5
Osteoblastic	122	37	8	21	3	2		2	1
Chondroblastic	34	29	25	8	3	5	2		2
Fibroblastic	42	26	7	6		3		1	2
Parosteal	16	2		3					
Ewing tumor	37	15	21	10	3	10	5		8
Malignant giant cell tumor	7	2	1	1					
Adamantinoma		5*							
Fibrosarcoma	15	12	7	4		1	4		4
Chordoma					15		43		
Hemangioendothelioma					2	1			
Total malignant	335	150	153	78	92	90	66	4	37
Total series	509	252	199	154	113	106	79	68	66

* One tumor involved both tibia and fibula.

Chapter 2

Osteochondroma (Osteocartilaginous Exostosis)

THIS MOST COMMON of the benign bone tumors logically belongs in the chondrogenic group Although the average osteochondroma is predominantly osseous, the bony mass is produced by progressive enchondral ossification of its growing cartilaginous cap Growth of these tumors usually parallels that of the patient, and they often become quiescent when the epiphyses have closed.

One may question whether osteochondromas are correctly classed with the neoplasms of bone, but their clinical features and their rare malignant transformation make it reasonable to include them among the tumors. Their pathologic features make it apparent that the tumors are produced by growth of aberrant foci of cartilage on the surface of bone Hence one could consider these tumors among the congenital anomalies.

Multiple Osteochondromas

A much smaller group of patients has numerous osteochondromas affecting many bones In this condition, which has a strong familial tendency each individual tumor has the characteristics that will be described for the solitary form. The incidence of development of secondary chondrosarcoma in patients with multiple osteochondromas is probably more than 10 per cent. Osteochondromas result from a distinctive form of dysplasia that should not be confused with enchondromatosis.

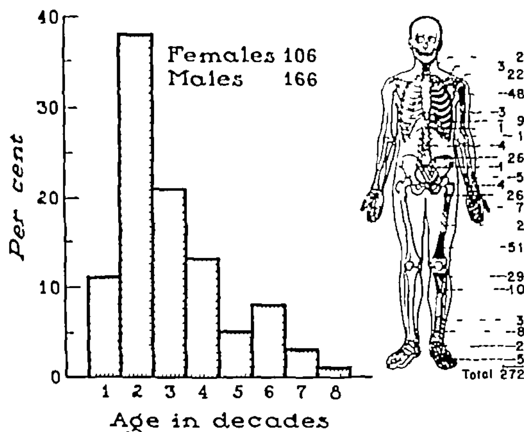


Fig. 1. Skeletal, age and sex distribution of osteochondromas

Incidence

Osteochondromas comprised 42.7 per cent of the benign bone tumors and 12 per cent of the total in this series. When it is considered that a large number of these tumors are asymptomatic and are never found, and that many of those discovered are not excised their actual incidence is much greater than these figures indicate.

Sex

A trifle more than 60 per cent of the patients in this series were males. The literature indicates little sex predilection.

Age

Nearly half of the patients were less than 20 years of age at the time of excision of their osteochondromas, and 38 per cent were in the second decade of life. The age distribution parallels that of osteogenic sarcoma.

Localization

Osteochondromas may occur on any bone that develops by enchondral ossification. They usually occur in the metaphyseal region of the long bones of the limbs, and nearly half of those in this series involved the femur and humerus. The scapula accounted for 2 tumors whereas the clavicle contributed only three, the ribs nine, and the vertebrae and sacrum eight.

Symptoms

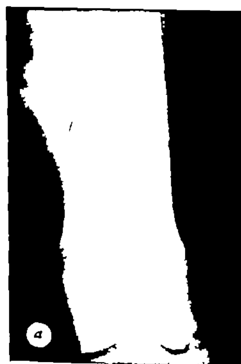
The patient's complaints are related to the size of the tumor the complaint of a hard swelling, usually of long duration, is the commonest. The presence of the mass may induce the patient, because of fear or vanity to seek medical care. Pain may result from the tumor's impinging on neighboring structures or from weight bearing or other activity

Physical Findings

Palpable mass is ordinarily the only finding. Secondary effects may occur especially when the tumor infringes upon the spinal canal

Roentgenologic Features

The characteristic appearance is that of a projection composed of a cortex continuous with that of the underlying bone and a spongiosa, similarly continuous. The adjacent cortex often flares to become the base of the tumor. The projection may have a broad base or be distinctly pedunculated. Irregular zones of calcification may be present, especially in the cartilaginous cap but extensive calcification with consequent irregularities of the cap should arouse the suspicion of malignant change. Osteochondromas commonly arise at the site of tendon insertions and the direction of their growth is often along the line of the tendon's pull. The affected bone is often abnormally wide at the level of an osteochondroma owing to failure of normal tubulation.



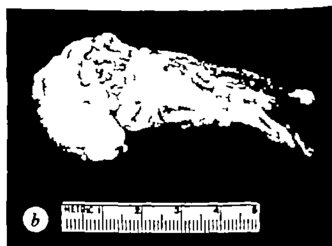


Fig 2 2. a (left) Pedunculated osteochondroma of the medial aspect of the femur b Gross specimen in the same case showing regular, smooth, cartilaginous cap



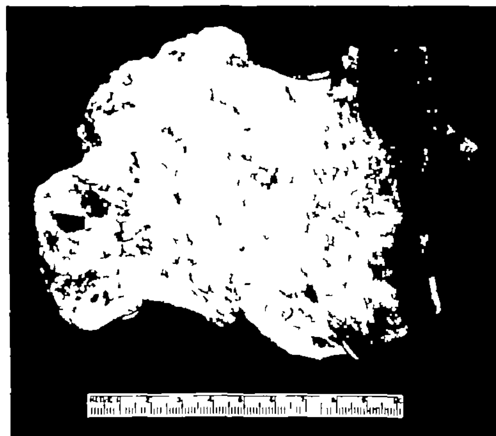








Fig. 2-4 (*above left*) Small hereditary multiple osteochondromas about the knee

Fig. 2-5 (*above right*) Sessile exostoses in one of the commoner sites. Gross specimen is shown in Figure 2-8.

Fig. 2-6 (*left*) Osteochondroma proved benign but with roentgenologic features suggestive of chondrosarcoma

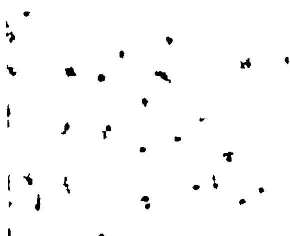


Fig. 11 M[illegible] [illegible] (×[illegible])

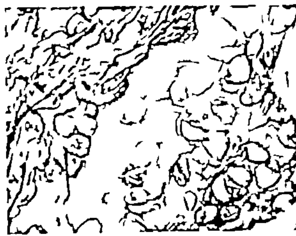


Fig. [illegible] C[illegible] dying [illegible] of degenerating cartilage in the stalk of an osteochondroma (× 1[illegible]0)

Treatment

The presence of an osteocartilaginous exostosis is in itself insufficient reason for surgical extirpation since malignant transformation occurs in only about 1 per cent of clinically recognized osteochondromas. Removal is indicated if the tumor is unsightly, is producing pain or disability, has roentgenologic features suggestive of malignancy, or shows abnormal increase in size.

Removal of the tumor flush with the bone of origin is the treatment when surgical intervention is indicated. The entire cartilaginous cap should be removed.

Although chondrosarcoma will develop in approximately 10 per cent of patients with multiple osteocartilaginous exostoses, the tumors are too numerous to allow prophylactic removal. The same general principles should govern removal of a tumor in this condition as in the solitary form of the disease.

Prognosis

Benign lesions will not recur if they are completely removed. Recurrence strongly suggests that secondary chondrosarcoma was already present at the time of excision, since it is rarely due to incomplete removal of a benign osteochondroma.

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Chapter 3

Chondroma

THIS BENIGN TUMOR is composed of mature hyaline cartilage. Most commonly chondromas are centrally located in bone, and such tumors are called "enchondromas." Less often they are distinctly eccentric and bulge the overlying periosteum; this type has been called "periosteal chondroma." In thin or flat bones such as the ribs, scapula or innominate bone, the exact origin of chondromas, that is, whether central or subperiosteal, often cannot be determined because of destruction of landmarks by the tumor.

Multiple Chondroma

This dysplasia of bone is characterized by failure of normal enchondral ossification with the production of tumefactive cartilaginous masses in the epiphyseal and adjacent regions of the shaft. A few or many bones may be affected. With widespread involvement and a tendency to unilaterality, this condition is often called Ollier's disease. In addition to tumefaction, there are concomitant bowing and shortening of bones as a result of this disease. In fact, multiple chondroma and fibrous dysplasia both result from disordered ossification, and this relationship is emphasized by lesions containing histopathologic features of both. Patients with multiple chondroma occasionally have osteocartilaginous exostoses as well, but skeletal osteochondromatosis and multiple chondroma are distinctive and separate entities. Completely reliable figures are not available, but approximately one third of the cases of multiple chondroma are complicated by chondrosarcoma.

Chondroma

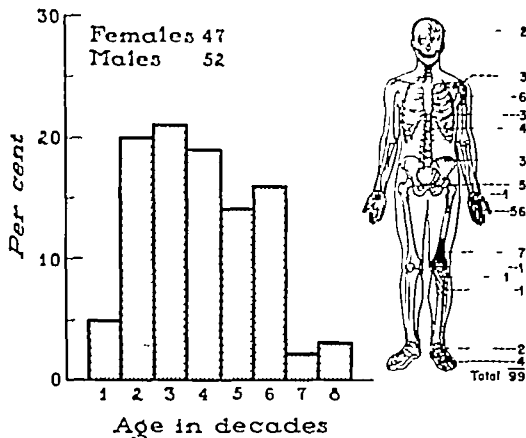


Fig. [illegible] Skeletal, age and sex distribution of chondromas.

Incidence

Chondromas comprised more than 15 per cent of the benign bone tumors of the present series and less than 5 per cent of the entire series.

Sex

Experience in the present series of cases bears out recorded data which indicate no significant sex predilection.

Age

Cases were fairly evenly distributed through the second to sixth decades of life inclusive, whereas cases were rare in the extremely young and old.

Localization

More than 60 per cent were in the hands and feet chiefly in the phalanges, and 90 per cent of these were in the hands. The innominate bone, ribs and scapula each accounted for three chondromas, and a carpal bone, the patella, tibia and fibula accounted for one each. Four were in vertebrae, and interestingly the temporal and parietal bones each accounted for one. Possibly the latter two tumors were of meningeal origin. The bones most commonly affected by chondrosarcoma are relatively immune to chondroma.

Symptoms

Many chondromas are asymptomatic, and this can be attributed to their extremely slow rate of growth. Some are discovered accidentally on roentgenographic examination. Pathologic fracture often ushers in the symptoms of the commonly seen chondroma of the distal portions of the extremities. Notable swelling is rarely produced. Pain unassociated with pathologic fracture should arouse the suspicion of malignancy because it suggests that the tumor is invasive.

Physical Findings

Physical examination contributes little to the diagnosis of chondroma of bone. Rarely is there tumefaction. The occurrence of pain or pathologic fracture merely directs one's attention to the appropriate region for roentgenographic study.

Roentgenologic Features

The average chondroma produces a well-circumscribed central region of rarefaction. Any portion of the small tubular bones of the hands and feet may be affected, but the tumor is ordinarily metaphyseal in location. From slight to very prominent stippled or mottled calcification of the tumor is frequently seen, especially in those chondromas occurring in the large tubular bones. The cortex overlying a chondroma is often expanded, and the expansion may be eccentric. The presence of calcification within a well-circumscribed rarefying tumor affords strong evidence that the lesion contains hyaline cartilage that is undergoing degenerative change. Some chondromas lie eccentrically beneath the periosteum, in a well-demarcated cortical defect.



Fig. 3-2 Typical central chondroma of a small bone, in this case affecting the distal phalanx of the thumb.



Fig. 3-3 Heavily calcified chondroma. Such density is ordinarily the result of calcification secondary to necrosis.





Fig. 3-4 (a/) Enchondromat (Ollier dyschondroplasia) with multiple deforming cartilaginous t mors with punctate calcification in the lesional ti ue. (Reproduced with permis on from Pugh, D. G. Roent ... Dis ... of Bon . Baltimore Williams and Wilkins 1954 pp 4 8-412.)

Fig. 3-5 (a/ g/t) Multiple deforming enchondroma

Fig. 3-6 (g/t) Large ubper st l hondroma lying in a typic l ... ity with scler sed ma gins





FIG. 3-7 Rare but markedly deforming multiple chondromas, in this case affecting only the hands. This may be a mild manifestation of Ollier's dyschondroplasia. Enchondromas of the hands usually produce no visible swelling. (Reproduced with permission from Shellito, J. G. and Dockerty, M. B., *Surg. Gynec. & Obst.* 86:465-472, 1948.)

Gross Pathology

The characteristic chondroma is composed of confluent masses of bluish, semitranslucent, hyaline cartilage with a distinctly lobular arrangement. The lobules vary from a few millimeters to a centimeter or more in diameter. The periphery of the lesion may be somewhat indistinct, because ramifications of the cartilaginous tumor sometimes penetrate into adjacent marrow spaces. Some of the tumors are very soft and mucinous. Those characterized by x-ray evidence of punctate areas of calcification have more or less densely calcified masses scattered throughout the tumor, and occasional lesions are heavily calcified and ossified. The gross characteristics of the solitary tumor and of the individual tumors of the multiple variety are similar.

As previously indicated, most chondromas are central in location, but some of them are under the periosteum and produce erosion of the underlying cortex and a bulge in the contour of the bone. These subperiosteal chondromas lie in an excavation in the bone, and their internal limits are marked by a thin sclerotic zone.

Chondromas are characteristically small tumors, and when one encounters a tumor of hyaline h t measures several centimeters in diameter one should check carefully for e

Treatment

Curettage filling the defect with bone chips if necessary is the usual treatment. After curettage, some recommend chemical cauterization of the cavity and collapse of the cortical bone over the defect. If the tumor is in a small bone such as a rib that can be sacrificed or is in the subperiosteal region of a large bone and it can be excised en bloc with a surrounding portion of normal bone that is the proper treatment. Such total excision is especially desirable when the possibility of malignancy cannot be excluded preoperatively Curettage is likely to leave fragments of a lobulated tumor behind so that the tumor can recur even if it is benign.

Prognosis

With the treatment outlined the prognosis in chondroma is good and recurrence is unusual even after curettage Occasionally however a tumor which seemed completely benign recurs, and the recurrent tumor is characterized, in rare instances, by increased anaplasia with obvious evidence of malignancy Frequently this apparent increase in cellular activity is actually the result of failure of correct interpretation of the original specimen sometimes the apparent discrepancy is accounted for by the fact that insufficient microscopic sections were made for complete evaluation of the original specimen. Actually in the case of chondroma of the hand, the lesion is so innocuous in the average case that cure can be expected even if the tumor is obviously not completely excised

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Chapter 4

Benign Chondroblastoma

BENIGN CHONDROBLASTOMA is one of the neoplasms of bone that has been rescued from the wastebasket of giant cell tumors and is now recognized as a distinct entity. The basic proliferating cells of this neoplasm are remarkably similar to those of a true giant cell tumor, but these cells have the ability to produce foci of chondroid matrix, making it reasonable to include chondroblastoma among the tumors of cartilaginous origin. Valls and co-workers have suggested a reticulohistiocytic origin for these tumors, but most people relate them to epiphyseal cartilage.

Although some of the features of this neoplasm were recognized previously, it was not until 1942 that the term "benign chondroblastoma" was introduced and its distinctive clinicopathologic features were delineated. The cellular zones of these tumors ordinarily contain at least a few mitotic figures. These, coupled with the chondroid zones, have frequently led to the erroneous diagnosis of malignant giant cell tumor. Actually, one of the main reasons for recognizing this entity is that clinically it is very nonaggressive even as compared to true benign giant cell tumor and it is readily curable.

The present studies and those of others have indicated that there is a close relationship between benign chondroblastoma and chondromyxoid fibroma. In common with most observers, my colleagues and I have recognized no malignant counterpart of benign chondroblastoma.

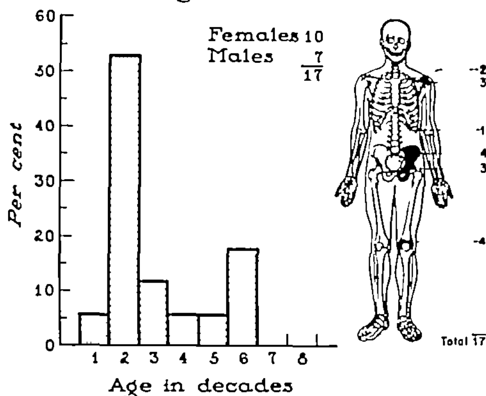


FIG. 4-1 Skeletal, age and sex distribution of benign chondroblastomas.

Incidence

Less than 1 per cent of this series of bone tumors were chondroblastomas, and they were one sixth as common as were true giant cell tumors

Sex

In more than 60 cases recorded in the literature males have predominated in a ratio of 2 to 1

Age

More than 80 per cent of the reported chondroblastomas have occurred in the second decade of life. In the present series several of the tumors were found in older patients and three of them were in patients more than 50 years of age

Localization

Chondroblastomas are characteristically epiphyseal in location Four of the tumors in this series occurred in the innominate bone and two in the scapula sites not previously reported as being involved by this neoplasm. Its occurrence in these bones is not inconsistent with an epiphyseal origin, since both contain several secondary centers of ossification One of the tumors occurred in a rib, and I have recently seen sections of another classic benign chondroblastoma in a rib.

Symptoms

Local pain is the most important and practically a constant symptom of benign chondroblastoma. It is often mild or moderate in degree as evidenced by the fact that patients of the present series had symptoms for 3 months to 16 years before they sought medical attention, and the average duration was slightly more than 2 years. The complaints are ordinarily referred to the adjacent joint region. Tumefaction is usually absent because of the small size of the tumor and the presence of overlying soft tissue.

Physical Findings

Aside from local tenderness which may be present the physical examination is of little diagnostic value. There may be wasting of the muscles in the region of the tumor owing to disuse, and limping may be observed. Some patients have increased fluid in the neighboring joint.

Roentgenologic Features

Characteristically this neoplasm presents with a central region of bone destruction which is usually sharply delimited from the surrounding normal bone by a thin margin of increased bone density. There may or may not be mottled areas of density within the radiolucent zone, depending on the presence and degree of calcification within the tumor. Both trabeculation and active periosteal reaction are rarely seen. The tumor when it involves the long bones almost always affects the epiphysis and frequently the adjacent metaphysis. Large chondroblastomas cause bulging and thinning of the cortex of the bone. The most important lesions that should be considered in the differential diagnosis roentgenologically are enchondroma, chondromyxoid fibroma, chondrosarcoma and benign giant cell tumor.



FIG. 4-2 (*above*). Small lytic chondroblastoma of the medial condyle of the femur.



FIG. 4-3 (*left*). Chondroblastoma measuring 5 by 3 by 2 cm. in the upper end of the humerus. Biopsy performed 18 days previously may account for the periosteal reaction. (Reproduced with permission from Kunkel, M. G., Dahlin, D. C. and Young, H. H.: *J. Bone & Joint Surg.* 38A:817-826, 1956.)

Treatment

Because chondroblastomas are so benign and nonaggressive the main danger is that too radical treatment may be instituted sometimes because of an erroneous diagnosis The pathologist who is not conversant with the features of this tumor is likely to mistake it especially for chondrosarcoma or for malignant giant cell tumor The average tumor of this type is best treated by curettage Bone grafting of the resultant defect may be necessary As in the management of other cartilaginous tumors, those chondroblastomas so located that they can be excised completely with a surrounding shell of bone should be so treated Radiation therapy is unnecessary and probably dangerous

Prognosis

Practically all chondroblastomas may be eradicated by the treatment outlined above. Even the rare tumor that recurs should not receive radical therapy It seems from the available evidence that irradiation is contraindicated The only well-documented benign chondroblastoma that has undergone malignant transformation was one that had irradiation as part of the primary therapeutic regimen.

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Chapter 5

Chondromyxoid Fibroma

Chondromyxoid fibroma is a rare and peculiar benign tumor apparently derived from cartilage forming connective tissue Its name, which is cumbersome, has the merit of being highly descriptive and is gaining acceptance for this distinctive tumor It was described by Jaffe and Lichtenstein in 1948 when they presented eight cases and emphasized the danger of mistaking this benign neoplasm for a malignant lesion, especially chondrosarcoma. The relative rarity of the neoplasm should not lull one into a complacent disregard for it, because anyone dealing with bone tumors must be prepared to interpret and manage any lesion he encounters. The fact is that one cannot ignore even the more complicated ramifications of a useful classification, because he cannot expect to diagnose and treat correctly a tumor with which he is unfamiliar.

Although chondromyxoid fibroma characteristically contains variable amounts of chondroid, fibromatoid and myxoid components, the fact that certain portions within the tumor resemble hyaline cartilage makes it logical to include this neoplasm among those of cartilaginous derivation.

The rationale of this classification is enhanced by the fact indicated previously that chondromyxoid fibroma and benign chondroblastoma sometimes having a striking histologic similarity

Many of the tumors referred to in the literature as myxomas and fibromyxomas of bone are, no doubt, examples of chondromyxoid fibroma.

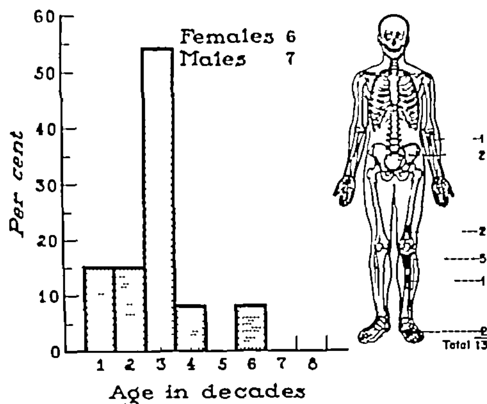


Fig. 51. Skeletal, age and sex distribution of chondromyxoid fibromas

Incidence

Chondromyxoid fibroma accounted for less than 1 per cent of the bone tumors of this series. Until 1956, only 28 cases had been reported in the literature

Sex

No sex predilection is yet apparent for this tumor

Age

More than 80 per cent of all the recorded cases have been in patients less than 30 years of age.

Localization

The typical chondromyxoid fibroma is located in the metaphyseal region of a bone and may abut on or be a variable distance from the epiphyseal line Occasionally a tumor involves both the metaphysis and the epiphysis This localization suggests that, like benign chondroblastoma, chondromyxoid fibroma possibly arises from the epiphyseal cartilaginous plate. The great majority of the recorded examples of this tumor have been in the long tubular bones with the tibia and femur contributing well over half of the cases. The small bones of the hands and feet however as well as the ribs and innominate bone have also given rise to this neoplasm

Symptoms

Pain is by far the most common presenting symptom of patients with chondromyxoid fibroma. Local swelling is occasionally a complaint of patients whose tumors are not camouflaged by a thick layer of overlying tissues. Such tumefaction had been noted by only three of the 13 patients in this series.

Physical Findings

Physical examination is of little diagnostic aid. Tenderness in the region of the tumor or a tender or nontender mass, may be found and aid in exact localization.

Roentgenologic Features

The roentgenogram, in addition to providing accurate localization of the lesion, strongly suggests the benign nature of this tumor in the average case. The defect is characteristically an eccentric, sharply circumscribed zone of rarefaction that occasionally causes expansion of the bone. The cortical outline was partially absent over three of the tumors of the present series. A chondromyxoid fibroma in a small bone can produce fusiform expansion of its entire contour.

Trabeculae appear to traverse the defect in most cases, but these are merely the roentgenographic reflection of corrugations on the inner surface of the cavity that contains the tumor. Sometimes the bone adjacent to the tumor is characterized by a thin delimiting line of sclerosis. Although a minority of these neoplasms contain microscopic foci of calcification, I have seen only one tumor of this type in which these foci were prominent enough to be reflected in the roentgenographic shadow.





FIG 3.2. Chondromyxoid fibroma that had caused pain for 8 months. There was tender swelling of the upper part of the ulna. *b* This tumor occurred in 8-year-old man and had produced local pain for 2 years. (Reproduced with permission from Dahlin, D C *Cancer* 9 195-203, 1956.)





FIG. 5-3. *a* Chondromyxoid fibroma in a 14-year-old girl who had had local pain for 3 months. *b* Lateral view of the same lesion. It recurred 20 months after curettage and was then treated by block excision. (Reproduced with permission from, Dahlin, D. C.: *Cancer* 9:193-203, 1956.)



FIG. 5-4. Chondromyxoid fibroma of the radius showing punctate calcification. (Case contributed by Drs. C. R. Dochat, Robert Fowler and Charles Miller of Akron, Ohio.)

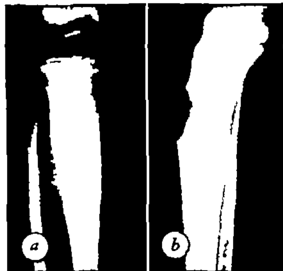


FIG. 5-5. and *b* Anteroposterior and lateral views of chondromyxoid fibroma in 10-year-old boy. Foci of chondroblastoma were present in the tumor. (Reproduced with permission from Dahlin, D. C.: *Cancer* 9:193-203, 1956.)

Gross Pathology

The average tumor of this type is small, those of this series varying in size up to 5 cm. in great diameter. *Grossly it may closely resemble hyaline cartilage or appear as a somewhat translucent fibrous ma* In general, the consistency is denser than one would suspect from the histologic appearance. A striki feature is the sharp delimitation from the surrounding bone, a feature which contrasts with what o observes in chondrosarcoma. The surface of the tumor is often distinctly lobulated and the cavity fr which it is enucleated frequently is characterized by corrugations that correspond with the tumor lobul There may be a thin sclerotized zone in the bone immediately adjacent to the neoplasm.

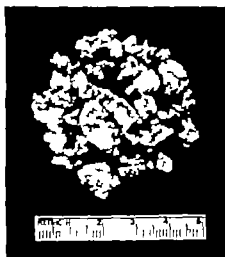


FIG. 3-6. Firm, fibrocartilaginous tissue removed by curettage from a lesion the roentgenogram of which is shown in Figure 3-2*b*



FIG. 3-7. Finely lobulated tumor enucleated from t defect represented in the roentgenograms shown in Figu 3-3*a* and *b*. (Reproduced with permission from Dahl D. C.: *Cancer* 9:195-203, 1956.)

Histopathology

The name of this tumor indicates the variation observed microscopically in different fields of a give tumor and from tumor to tumor. The gamut includes myxomatous zones, fibrous zones and fields with distinctly chondroid appearance. *The nuclei of the cells are round, oval or spindle-shaped. The chondroi* element may occupy only small foci but it occasionally dominates the histologic picture and introduces th hazard of mistaking the tumor for a chondrosarcoma. Chondromyxoid fibroma characteristically possesse a lobular pattern of growth but this feature is sometimes obscured in microscopic sections prepared fro curetted fragments, and the lobules are often only partially separated from each other. A highly char acteristic feature is the increased concentration of nuclei observed at the periphery of the lobules and partia lobules. At the edge of the tumor this cellular peripheral zone is sharply demarcated from the surroundin uninvolved tissues. Variable degrees of collagenization of the lobules are observed. Small amorphous foc of calcification are occasionally present and these sometimes have the lacelike quality of the calcificatio seen in benign chondroblastoma. Benign giant cells and phagocytic mononuclear cells may be seen in th

tissue between the lobules. As indicated in the preceding chapter some chondromyxoid fibromas contain cellular foci indistinguishable from microscopic fields in benign chondroblastoma.

The most important histologic feature of chondromyxoid fibroma is that the cells in some portions of many of these tumors are large and have nuclei of irregular size and shape and even contain multiple nuclei at times. These features, if present in a hyaline-cartilage tumor of the chondroma-chondrosarcoma group would be indicative of malignancy. When one recognizes, however that these cells are only part of the over-all pattern of chondromyxoid fibroma, the benign nature of the lesion is firmly established.





Fig. 5-8 (*above left*) Cross section of entire tumor which had caused some expansion of rib (×6) (Reproduced with permission from Dahlin, D. C. *Cancer* 9:195-203 1956.)

Fig. 5-9 (*above right*) Periphery of tumor lobule showing characteristic condensation of nuclei beneath the rim of compressed adjacent tissue, here located above the neoplastic tissue (×150) (Reproduced with permission from Dahlin, D. C. Wells, A. H. and Henderson, E. D. *J Bone & Joint Surg* 35A 831-834, 1953.)



Fig. 5-10 (*right*) Chondroid zone of the type commonly seen in chondromyxoid fibroma (×200) (Reproduced with permission from Dahlin, D. C., Wells, A. H. and Henderson, E. D. *J Bone & Joint Surg* 35A 831-834, 1953.)





FIG. 5-11 *a* Well-demarcated periphery showing fibromatoid and chondroid features (×180) *b* Myxoid zone of the type seen in many chondromyxoid fibromas (×200) (Reproduced with permission from Dahlin, D. C., Wells, A. H. and Henderson, E. D *J Bone & Joint Surg* 35A 831-834, 1953)





FIG. 5-1[illegible] Focus showing marked nuclear atypism in a chondromyxoid fibroma. Such zones have no significance in lesion that has the other features of this benign tumor (×320) *b* Tumor lobule separated, in this plane, from the main neoplasm. Such [illegible] foci could be left behind during curettage and thus account for recurrence (×40) (Reproduced with permission from Dahlin, D C *Cancer* 9 195-203, 1956)

Treatment

Removal of the tumor by curettage with bone grafting of the resultant cavity if indicated is the usual treatment employed. For those lesions so located that they can be excised en bloc, that is the treatment of choice. Radiation therapy is not indicated.

Prognosis

Chondromyxoid fibroma is so completely benign that total removal by curettage ordinarily effects a cure. At least two tumors of this type have recurred following conventional curettage. Such recurrence can be explained on the basis of the lobulation of the periphery of the tumor which may lead one to leave a ramification of the tumor behind when he removes it by curettage. For this reason it is wise to remove the tumor along with a margin of uninvolved bone whenever possible.

No instance of malignant transformation of chondromyxoid fibroma has been reported.

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Chapter 6

Osteoma

THE ACTUAL OCCURRENCE of true osteoma is so debatable that this tumor was not included in the over-all statistical data. Reactive changes from trauma, infection or invading tumor such as meningioma can cause osseous overgrowth. Since these tumefactions produce the clinical manifestations of a neoplasm they are often erroneously called "osteomas."

Occasional tumors of the skull, especially those involving the paranasal sinuses, are the most nearly bona fide osteomas, and yet there is room for conjecture regarding these. The gamut of fibro-osseous dysplastic lesions that affect these bones runs from soft, purely fibrous lesions to those that are heavily ossified. Hence, there is no clear line of distinction between obviously dysplastic lesions and completely osseous tumors that one might wish to call "true osteomas."

Rarely one encounters a sessile ossified neoplasm on the surface of a bone, a tumor with roentgenologic and pathologic features that relate it closely to the malignant tumor called "parosteal osteogenic sarcoma." These benign counterparts are best regarded as parosteal osteomas.

Because of the hodgepodge of tumors included among the "osteomas" no attempt will be made to discuss their features as a group. Some of the characteristics of three pertinent types will be illustrated.



FIG 6-1 Osteoma of the frontal sinus in a 19-year-old boy It had produced local tumefaction. Such lesions can produce symptoms by blocking drainage from the sinus or by penetrating into neighboring structures, including the cranial cavity



FIG 6-2 Densely ossified osteoma Reactive bony sclerosis can give similar appearance (×60)



FIG. 6-3 Gross specimen removed from the patient whose roentgenogram is illustrated in Figure 6-1

Fig. 6-4. a and b Anteroposterior and lateral views of a dense parosteal osteoma of the tibia of a 43-year-old man who had noted gradually increasing swelling for 31 years. This tumor bears roentgenographic resemblance to parosteal osteogenic sarcoma.

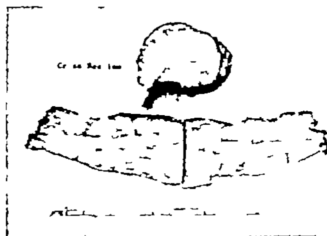
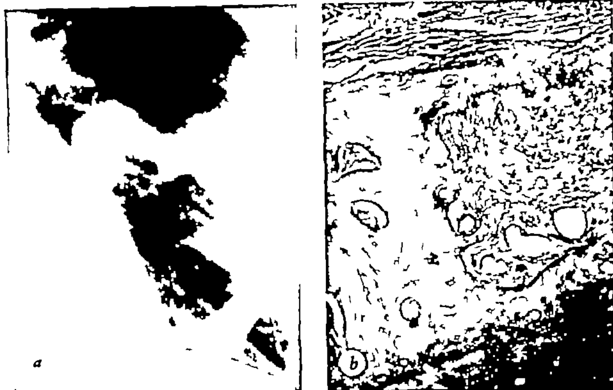


Fig. 6-5 Tumor illustrated in Figure 6-4 above. It was excised along with the subjacent cortex of the bone.



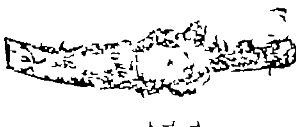


Fig. 6-6. *a*. Irregular sessile osteoma of the eighth rib. This was an incidental finding, having produced no signs or symptoms. *b* Periphery of the same lesion showing that the osseous tissue appears to be derived from proliferating fibroblasts, apparently by a process of metaplasia. This appearance is reminiscent of what one commonly observes in parosteal osteogenic sarcoma (×70) *c* (*below*) Excised specimen.

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Chapter 7

Osteoid Osteoma

THE MAJORITY OPINION now favors the view that osteoid osteoma is a neoplasm and not the result of some obscure infection or other known specific etiologic agent. This distinctive benign osteoblastic lesion consists of a small oval or round mass, commonly called a nidus. This nidus is often associated with a surrounding zone of sclerotic bone especially when the lesion develops in a cortical portion of bone. The nidus is the essential part of the tumor the surrounding sclerosis being a reversible change which disappears after removal of the nidus. As will be illustrated, the major component of this tumor is a meshwork of osteoid trabeculae showing varying degrees of mineralization in a background of more or less vascular fibrous connective tissue.

Certain instances of focal subacute or chronic osteomyelitis in bone produce a clinical and roentgenographic picture that has been confused with that of osteoid osteoma, especially when these inflammatory lesions are associated with a small, discrete, central rarefied focus. Histologically of course, the lesion produced by inflammation and that by genuine osteoid osteoma are readily distinguished when appropriate sections are made.

For a neoplasm, osteoid osteoma has a strangely limited growth potential and tumors more than 1 cm. in largest diameter are unusual.

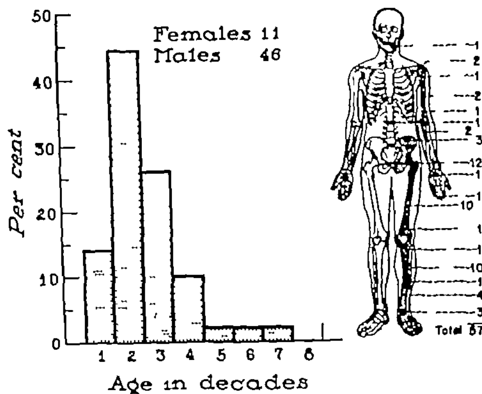


Fig. 7 1 Skeletal, age and sex distribution of osteoid osteomas.

Incidence

The 57 osteoid osteomas in the present series comprised 9 per cent of the benign bone tumors. This is undoubtedly lower than the actual incidence, because this type of tumor was not commonly recognized until recent years.

Sex

Like others, my colleagues and I have noted a predominance in males, our ratio of males to females being 4 to 1.

Age

This tumor has a predilection for the younger age group that parallels closely that of osteogenic sarcoma. The youngest patient in this series was 21 months old. The peak incidence is in the second decade of life

Localization

Osteoid osteoma most commonly affects the lower extremities. In this series three were observed in the innominate bone, one in a vertebra, two in the scapula and one in the mandible. The literature is difficult to evaluate because of the inclusion of examples of giant osteoid osteoma (next chapter) but it indicates a higher incidence of vertebral involvement than was observed in the present series

Symptoms

By far the most important complaint is pain of gradually progressing severity. Its duration prior to the patient's seeking medical care may vary from weeks to several years. Many have noted that salicylates relieve the pain which otherwise commonly interferes with sleep. The pain is often referred to the adjacent joint region and occasionally it is referred to a site so distant from the lesion that roentgenographic studies are misdirected. In some instances, especially when the bone involved is near the skin, local swelling may become evident.

Physical Findings

Dysfunction, often resulting in a limp, is commonly produced by an osteoid osteoma. Atrophy of some muscles of the affected extremity was noted in more than half of the osteoid osteomas of the extremities in the present series. This atrophy rarely produced significant weakness.

Sharply localized tenderness has been a more common feature in some series of osteoid osteomas than in the present series.

Roentgenologic Features

In the average lesional region there is thickening of the cortex mainly on its periosteal surface. A variable portion of the involved bone is affected. The nidus is ordinarily located near the center of the zone of sclerosis and sometimes is demonstrable only by means of special roentgenographic technics. It appears as a round or oval area of decreased density which sometimes has a central area of increased density. Sclerosis of the nidus itself adds to the problem of roentgenographic visualization.

In some cases the typical clinical symptoms precede the onset of recognizable roentgenographic changes. It should also be emphasized that some osteoid osteomas, especially those in cancellous bone, show little or no perifocal sclerosis. This absence of sclerosis in some cases makes the roentgenographic picture of ordinary osteoid osteoma merge with that of giant osteoid osteoma, to be discussed in the next chapter.



Fig. 7.2. Osteoid osteoma of the triangular bone of the wrist. The center of the nidus is denser than the periphery and there is only slight sclerosis of the bone around the lesion. There was only one osteoid osteoma of the wrist bone in the present series prior to 1956, but several have been reported in the literature.





FIG. 7-3. and *b* (*above*) Anteroposterior and lateral views of an osteoid osteoma of the femur showing the typically small nidus with considerable sclerosis of the adjacent bone.



FIG. 7-4 (*right*) Another typical osteoid osteoma in the cortical region

Gross Pathology

Whether the osteoid osteoma is found in relatively nonsclerotic cancellous bone or buried in a large region of cortical sclerosis, the actual nidus, upon exposure, stands out as a discrete round or oval mass of tissue. It is ordinarily redder than the surrounding bone and can be lifted from its bed. The nidus itself varies in consistency from soft and granular to densely sclerotic, the more heavily calcified, sclerotic lesions apparently being the older ones. Sclerosis, when present, is usually most marked in the central portion of the nidus. Osteoid osteoma has, as previously noted, a peculiarly limited growth potential, which is an unusual feature of true neoplasms. The nidus of this type of tumor is, as previously indicated, usually less than 1 cm. in diameter.

When the sclerotic zone including the nidus is chiseled indiscriminately from an affected bone it is difficult or impossible for the pathologist to find the all important central mass of tumor tissue, without which the diagnosis cannot be established. It is important, therefore, that the surgeon remove the nidus intact for satisfactory pathologic appraisal. If the tumor is identified as such and is demonstrated to be completely removed, both the diagnosis and prognosis are established.



FIG. 5. Osteoid osteoma removed en bloc from the neck of the femur of 21-year-old man who had had pain in the hip for 1 year. Photomicrographs of the lesion are shown in Figures and 10.



Osteoma

FIG. 7-6. Typical osteoid osteoma from an unusual site the mandible. This occurred in 26-year-old woman whose chief complaint was pain in the jaw. Some lesions of fibrous (fibro-osseous) dysplasia of jawbones closely simulate the histologic appearance of the nidus of an osteoid osteoma.

Treatment

The treatment is surgical removal of the nidus. It is important that the nidus be entirely removed and one should probably include at least a thin margin of adjacent bone Whenever possible the nidus and some surrounding bone should be removed en bloc

Roentgenographic guidance may be necessary at the time of operation It is not necessary to remove all of the thickened bone around the osteoid osteoma proper since this zone will resolve spontaneously if the entire nidus is gone.

Prognosis

Complete removal of the focus of tumor tissue results in cure. Incomplete removal of this focus may lead to recurrence of symptoms and the necessity for reoperation. Whether a true osteoid osteoma will resolve without surgical intervention is unknown The cases in which such a course seems to have occurred have not had pathologic verification of the original diagnosis.

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Chapter 8

Giant Osteoid Osteoma (Osteogenic Fibroma, Benign Osteoblastoma)

THE LITERATURE concerning this rare, benign tumor is especially confusing. Its osteoblastic nature results in zones often quite like those of an ordinary osteoid osteoma, producing a histologic kinship that can scarcely be ignored. Giant osteoid osteoma differs, however in not sharing the markedly limited growth potential of the average osteoid osteoma. Further it frequently lacks the characteristic pain and the halo of sclerotic bone of the latter tumor Even so one occasionally encounters a lesion whose composite features make it fall midway between the two lesions under discussion.

In the literature dealing with neoplasms of the vertebral column, giant osteoid osteoma is found under a variety of diagnoses including giant cell tumor osteoid osteoma, osteogenic (or ossifying) fibroma, and sarcoma. An important reason for recognizing this entity is that it has commonly been mistaken for the much more aggressive, genuine giant cell tumor or even for sarcoma.

One may logically question whether giant osteoid osteoma is correctly classed with true neoplasms since some of them regress or become arrested after incomplete surgical removal. Fields within some of these tumors resemble portions of aneurysmal bone cysts. This coupled with a pronounced clinical similarity suggests that both of these processes may be but different manifestations of a reaction to some as yet unknown agent.

Benign osteoblastoma is another name that has been suggested recently for this type of tumor

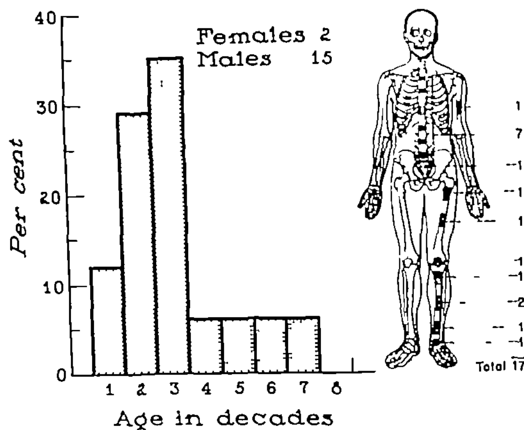


Fig. 8-1. Skeletal, age and sex distribution of giant osteoid osteoma.

Incidence

This tumor accounted for less than 1 per cent of the primary tumors of bone in the present series, but it is being diagnosed somewhat more frequently in recent years.

Sex

In this series the tumor showed a definite predilection for males, but too few cases have been reported to determine the true sex incidence

Age

This tumor appears to be distinctly one of the younger age group and all but four in this series were in patients in the first three decades of life

Localization

Giant osteoid osteoma, in contrast to all other neoplasms of bone except myeloma and chordoma, manifests a distinct predilection for the vertebral column. Eight in this series affected the spinal column and sacrum. The remainder were in the long bones except for one tumor in the patella and one in the talus.

Symptoms

Pain, usually at the site of the tumor is the cardinal symptom. In many instances the pain is due to pressure on adjacent structures, notably the spinal cord or the emerging nerves, and it appears to lack the intrinsic severity of that caused by ordinary osteoid osteoma. Involvement of the spinal cord or nerves may result in weakness or even paraplegia The pain may be referred to a site distant from the tumor The lesion develops slowly the average duration of pain in the present series was 25.8 months before the patient sought medical advice. If the affected bone is not covered by a thick layer of soft tissue, local swelling may be evident. Those patients with a lesion in the lower extremity may experience a limp.

Physical Findings

Physical examination is of little value in the definitive diagnosis of this lesion, but it may reveal a tender mass at the site of the tumor Atrophy of the adjacent muscles is sometimes seen. Variable neurologic deficits may be noted, depending upon the degree of involvement of the spinal cord or emerging nerves.

Roentgenologic Features

The roentgenologic picture is not as characteristic in this tumor as it is in ordinary osteoid osteoma. In some cases all one observes is bone destruction that is more or less well circumscribed and does not always suggest that the process is benign. In some instances, especially in the long bones, the lesional site is surrounded by a dense sclerotic zone similar to that seen in ordinary osteoid osteoma. The main difference from ordinary osteoid osteoma is that the region of the central nidus is almost always many times larger in these cases. Many giant osteoid osteomas arise in bones that are predominantly cancellous and this may help account for the common absence of perifocal sclerosis. Occasionally the tumor is surrounded by a thin layer of bone beneath an expanded periosteum, giving an appearance similar to that of aneurysmal bone cyst some of Lichtenstein's benign osteoblastomas showed this feature. In older or previously treated lesions, more or less ossification of tumor tissue results in enough radiopacity to cause the roentgenologist to consider that the tumor is an osteoma



FIG. 8-2. Example of this tumor type. It has produced some expansion of the right transverse process of the seventh cervical vertebra The excised specimen measured 2 cm. in diameter.



FIG. 8-3 The left tibia on September 1 1943, showing a barely visible radiolucent area surrounded by dense sclerotic bone *b* Same lesion on January 17 1946 after three drilling operations elsewhere, each of which brought temporary relief *c* Excised tumor and anterior half of tibia. The tumor showed classic features of giant osteoid osteoma. (Reproduced with permission from, Dockerty M. B., Ghormley R. K. and Jackson, A. E., *Ann Surg* 133 77-89 1951)



FIG 8-4 A completely lytic giant osteoid osteoma 2.5 cm. in diameter as removed 6 years previously from the site of this now sclerotic and asymptomatic tumor



FIG. 8-5 The 32-gm. tumor shown in Figure 8-7 was removed from this talus (Reproduced with permission from Dahlin, D C. and Johnson, E. W Jr *J Bone & Joint Surg* 36A:559-572, 1954)

Gross Pathology

The gross pathologic features of this tumor are relatively characteristic. Entire gross specimens are rarely observed because the average lesion is removed by curettement. These tumors are, however reasonably well circumscribed. The tumor tissue is hemorrhagic, granular and friable, owing to its vascularity and its osteoid component which shows variable degrees of calcification. In some of the older lesions the consistency resembles that of cancellous bone, and decalcification is necessary before microscopic sections can be made. If the tumor bulges from and distorts the contour of the affected bone, its margins are sharply defined. The limited data that are currently available regarding this tumor strongly suggest that young lesions are distinctly lytic, but that they undergo progressive ossification.

As previously indicated, the bone adjacent to a giant osteoid osteoma often is not sclerosed. Around the tumor in some cases there is a thin sclerotic rim, and around the tumor proper in others, especially those in the long bones of the extremities, there may be a zone of increased density that is as prominent as that associated with ordinary osteoid osteoma.



Fig. 8-6 Cut surface of giant osteoid osteoma removed from the sacrum of a 22-year-old man who had had local pain for 3 years. It measured 4 by 3.5 by 3 cm. This predominantly lytic lesion involved the left lower part of the sacrum.



Fig. 8-7 Curetted fragments of the tumor the roentgenogram of which is illustrated in Figure 8-3. (Reproduced with permission from Dahlin, D. C. and Johnson, E. W. Jr.: *J. Bone & Joint Surg.* 36A: 559-572, 1954.)

Histopathology

The microscopic features of giant osteoid osteoma are extremely variable and account for the confusion in the literature regarding this tumor. In what are apparently early lesions one observes actively proliferating connective tissue which may show only slight osteoid formation and numerous giant cells. In the older ones, considerable ossification may be present. This variety accounts for the inclusion of cases of this type among the giant cell tumors, osteogenic fibromas, osteoid osteomas and osteomas. In the less mature lesions, mitotic figures are found in the actively proliferating cells, some of which may be obviously osteoblastic, hence the occasional confusion of this benign process with osteogenic sarcoma. Most of the giant osteoid osteomas contain numerous blood vessels, mainly of dilated capillary type, a feature which poses the question of vascular origin for this tumor.

Some of the lesions under discussion exhibit features of aneurysmal bone cyst. I have observed tumors in which some of the histologic sections were identical with those from an aneurysmal bone cyst, whereas other sections were typical of giant osteoid osteoma. This reinforces the interesting speculation as to whether both of these two rather poorly understood processes are related, a possibility that is enhanced by the similar age and skeletal distribution of these two tumors and their similar response to therapy.



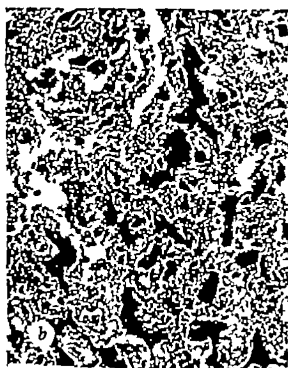


FIG. 8-8. *a*, Giant osteoid osteoma illustrated in Figure 8-7. The trabeculae of osteoid show no calcification in this area. Vascularity and benign giant cells are prominent (×170). *b*, Black areas indicate calcification of trabeculae. Giant cells are present (×100). (Reproduced with permission *from* Dahlin, D. C. and Johnson, E. W., Jr.: *J. Bone & Joint Surg.* 36A:559-572, 1954.)

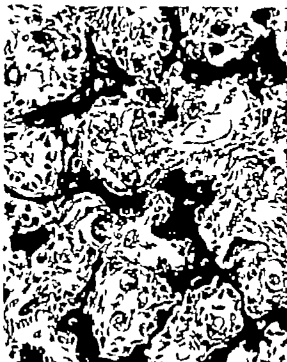




FIG 8-9 *a*. Giant osteoid osteoma with partially ossified trabeculae and prominent vascularity (×200) *b*. Vertebral tumor in this group showing distinct demarcation from the expanded and attenuated cortex on the right (×35) (Reproduced with permission from Dahlin, D. C. and Johnson, E. W. Jr. *J Bone & Joint Surg* 36A:559-572, 1954.)



FIG. [illegible] [illegible] giant osteoid osteoma, presumably an early [illegible] This type is likely to be mistaken for sar[illegible] [illegible] [illegible] production (×[illegible])



FIG 8-11 Persistent lesion involving a vertebra and showing, in this area, rather dense sclerosis. Giant cells are still abundant (×110)

Treatment

The benign nature of giant osteoid osteoma dictates that conservative surgical treatment be used. This will usually entail removal of the entire lesion, or as much of it as possible, by curettement, with bone grafting of the defect if indicated. There is no good evidence that radiation therapy is helpful. In some of the cases in the present series incomplete surgical removal of the lesional part has resulted in cure. The clinical course in the present cases suggests that until surgical intervention has been undertaken the tumefaction increases.

Prognosis

Perhaps the main reason for recognizing this rare pathologic entity is that it is not malignant and, as indicated, the response to treatment is nearly always good. Occasional tumors of this type that are incompletely removed will require more than one surgical procedure. The major problem likely to be encountered is that of involvement of the spinal column by a lesion; when this occurs one must direct therapy to preservation of the integrity of the spinal cord and the emerging nerve roots.

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Chapter 9

Benign Giant Cell Tumor (Osteoclastoma)

BENIGN GIANT CELL TUMOR of bone is a distinctive neoplasm of poorly differentiated cells The multinucleated, giant cells apparently result from fusion of the proliferating mononuclear cells and although they are a constant and prominent part of these tumors, they are likely of less significance than are the mononuclear cells. In fact, these osteoclastlike giant cells, with or without minor modifications occur in a host of pathologic conditions of bone. The ubiquitous giant cell accounts for the confusion one finds in the older and in some of the recent, literature on giant cell tumors. Authors have included conditions such as nonosteogenic fibroma, benign chondroblastoma, chondromyxoid fibroma, unicameral bone cysts with a cellular lining, giant cell reparative granuloma (epulis), aneurysmal bone cyst, hyperparathyroidism, giant-cell-containing osteogenic sarcoma and other entities in the general category of giant cell tumor Inclusion of these "variants" with their widely divergent biologic behavior has greatly delayed understanding of the clinical features and response to treatment of true giant cell tumor The exact cell of origin of this neoplasm is unknown.

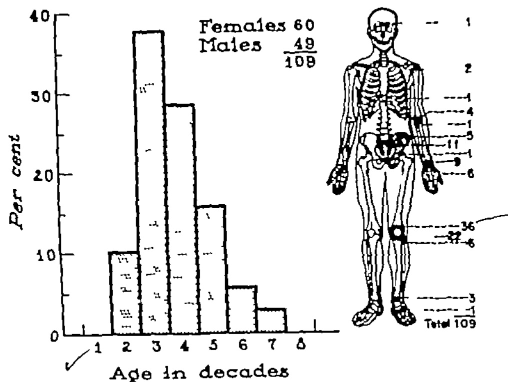


FIG. 9-1 Skeletal, age and sex distribution of giant cell tumors.

Incidence

The 109 cases in this series represented 4.8 per cent of the bone tumors and 17.1 per cent of the benign tumors.

Sex

In many of the recorded series, females have predominated. The ratio in the present series was 60 females to 49 males. This contrasts with the predominance of males in most series of other bone tumors.

Age

When the "variants" of giant cell tumor are excluded, 90 per cent of the neoplasms occur in patients beyond the age of 19 years, with the peak incidence in the third decade of life. Most of those in the second decade are nearly 20 years of age.

Localization

Most giant cell tumors are found in the epiphyses of the long bones. More than half of those in the present series occurred about the knee. The sphenoid, a rib, the upper part of the ulna, the upper part of the femur and a tarsal bone accounted for one each. Nine were in the lower part of the radius and six in the lower part of the ulna. Five occurred in the innominate bones and 11 in the sacrum. No verified giant cell tumor of the remainder of the spinal column was encountered, but subsequent to the tabulation of these data one bona fide example in a lumbar vertebra has been seen.

(1) Pain
(2) weakness
(3) limitatn of movtt
(4) fracture

Symptoms

Pain of variable severity is almost always the predominating symptom. More than three fourths of the patients in the present series had noted swelling in the affected region. Less common symptoms included weakness limitation of motion of a joint and symptoms of pathologic fracture

Physical Findings

A hard, sometimes crepitant and sometimes painful, mass is found in more than 80 per cent of patients. There may be atrophy of muscles due to disuse, effusion into the adjacent joint or local heat and redness

swelling, temp pain, crepitatns
effusion atrophy of musc

Roentgenologic Features

According to Gee, these features may be summarized as those of an expanding zone of radiolucency situated eccentrically in the end of a long bone of an adult. Such an appearance is neither specific for giant cell tumor nor produced by all such tumors The roentgenographic appearance may have been altered by pathologic fracture or by previous therapy The margin between tumor and normal bone is characterized by gradual alteration of density and there is no reactive sclerosis at this junction in untreated tumors. Gee was unable, after studying the available original roentgenograms of 62 of the patients in the present series, to correlate the roentgenographic features with the subsequent behavior of the tumors.



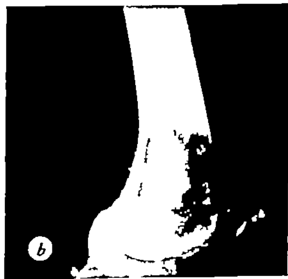


FIG. 9 Giant [illegible] tumor of lower end of femur of 21 year-old woman who had noted local pain for 9 months *b* Lateral view of same tumor

Treatment

Removal of the tumor by curettage is the most widely accepted type of therapy. Many advocate chemical or thermal cautery of the walls of the cavity, and the defect is ordinarily filled with bone chips. Total excision of the tumor and its surrounding shell of bone and periosteum is sometimes the treatment of choice, especially when a small bone such as the fibula or radius is involved. Again, grafting may be required. In some of the massive lesions with marked destruction of juxta-articular bone, primary amputation is necessary. Some believe that, after multiple recurrences, amputation or radical excision should be considered because of the hazard of malignant transformation.

Irradiation as primary therapy has its advocates but is falling into disfavor because of its potential danger of inducing malignant transformation and the recognition that true giant cell tumors are radio-resistant. It has been commonly employed as an adjunct to surgical therapy.

Prognosis

Curettage was followed by recurrence in more than 50 per cent of the cases in the present series. Size of tumor, bone involved, preoperative duration of symptoms, cauterization of tumor cavity, bone grafting, cellular appearance and adjunctive irradiation therapy have no recognizable influence on the recurrence rate.

Amputation or total excision has been uniformly curative, but amputation is rarely indicated as primary treatment.

Secondary malignant change, usually in the form of pure fibrosarcoma or osteogenic sarcoma, occurs in approximately 10 per cent of benign giant cell tumors. Eight of the 11 malignant tumors in this series occurred an average of 7 years after verification of benign giant cell tumor and therapy which included irradiation in each instance. Six of these eight patients died as a result of metastasis, and two were cured by amputation. In one patient a sarcoma developed 1½ years after curettage and bone grafting without irradiation, and two patients had sarcomas present in portions of typical benign giant cell tumors at the time of their first operation.

Original sections from those benign giant cell tumors that recurred or from which secondary sarcomas developed were histologically indistinguishable from those cured by one surgical procedure. Grading of these tumors as to degree of malignancy has been of no prognostic value in the author's hands.

Metastasis from benign giant cell tumor occurs very rarely, and none was observed in our series.

Follow-up data on the results of treatment in this series are detailed on the following pages.

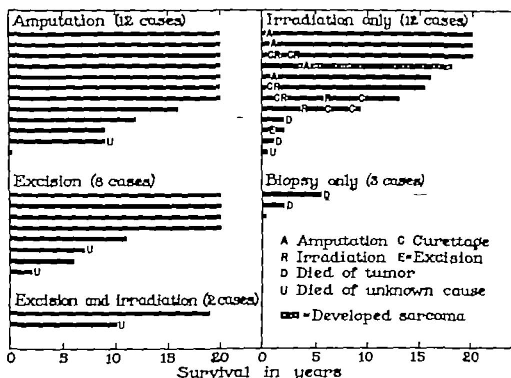


FIG. 9-13 (above) and 9-14 (opposite page). Follow-up data on 101 patients with giant cell tumor of bone. Each bar represents one case. The data available on each patient are plotted out to a maximum of 20 years from the time of performance of the procedure indicated by the appropriate group heading (for example, amputation—12 cases), no complication having developed in patients followed longer than that. The bars indicative of periods of less than 20 years and followed by no symbol represent patients followed to the time of these observations or lost to follow-up. Unbroken bars indicate no recurrence. Symbols inserted in the broken bars indicate the time of recurrence and the type of treatment. Symbols at the end of the bars indicate the final outcome. (Reproduced with permission from Williams, R. R., Dahlin, D. C. and Ghormley R. K. *Cancer* 7:764-773, 1954.)

It will be noted in Figure 9-14 (opposite page) that 31 patients were treated initially by curettage alone and 33 by a combination of curettage and irradiation. The cases shown in the two columns were similar in every respect in so far as could be determined. The size and histologic appearance of the tumors were similar and the rates of recurrence in the two groups were practically identical. Several of the patients treated primarily by amputation (Figure 9-13) were seen prior to 19 0 when all giant cell tumors were considered to be malignant. It should be noted that all of those in the series included in Figures 9-13 and 9-14 in whom sarcoma developed had irradiation therapy at varying intervals before malignant change occurred.

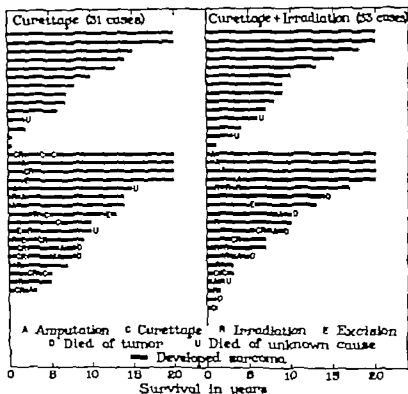


FIG. 9-14.

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Chapter 10

Fibroma (Nonosteogenic Fibroma, Fibrous Defects)

FIBROMA OR NONOSTEOGENIC FIBROMA is the name rather commonly applied to a rarefying lesion that ordinarily affects the metaphysis of a long bone. Since this tumor is benign and often asymptomatic, and yet is rarely found in adults, one might presume that it can be self-healing. Specific cases bear out this assumption, and some observers prefer to consider the lesion to be the result of a local defect of growth rather than being a true neoplasm. I favor the former view but because of common usage I have included fibromas of bone with the neoplasms.

Despite the innocuous clinical behavior of this lesion its component of benign multinucleated cells has frequently resulted in its being erroneously included in series of genuine giant cell tumors of bone.

It is pertinent to point out that one occasionally sees fibrous defects of bone that lack the cellularity and roentgenologic features of typical fibroma. The exact nature of some of these is obscure. Some may result from old trauma, hemorrhage or infection and some may represent the end stage or scar of an ordinary fibroma. Such lesions in the files of the Mayo Clinic have been tentatively grouped with the fibromas.

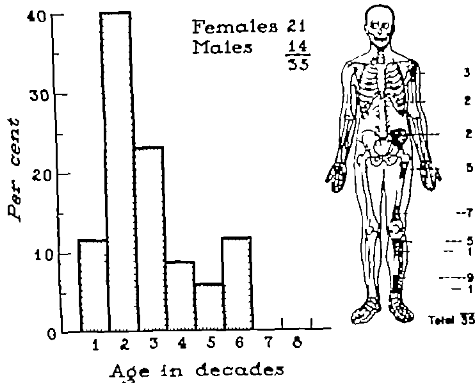


Fig. 10-1 Skeletal, age and sex distribution of fibromas.

Incidence

Although fibromas constituted only 3.5 per cent of the benign bone tumors in this series, their true incidence is much greater because the majority of them never come to operation.

Sex

Although females predominated in the present series, the literature indicates that the tumor is about equally common in the two sexes.

Age

This is chiefly a lesion of the younger age groups. Some of the lesions in older patients of this series were the atypical ones alluded to in the introductory part of this chapter.

Localization

The metaphyseal regions of the long bones, especially of the lower extremity, are most commonly affected. Only two of the lesions in this series involved the fibula and two were in ribs.

Symptoms

This lesion is commonly silent clinically and is discovered accidentally when a region is subjected to roentgenographic study for unrelated reasons. Local pain, usually of short duration, is sometimes produced. Occasionally especially in slender tubular bones such as the fibula, pathologic fracture ushers in the clinical symptoms. Overgrowth of the affected bone, possibly related to operative intervention, has been observed.

Physical Findings

Physical examination is of little diagnostic value in fibroma of bone. In rare instances slight swelling may be observed if the affected bone is near the surface of the body

Roentgenologic Features

Most fibromas present a characteristic roentgenographic appearance which is virtually pathognomonic. When a large tubular bone is affected the lesion is practically always eccentrically located and often produces some bulging of the cortical outline which is usually very thin over the defect.

The tumor begins in the metaphysis, near or at the epiphyseal line, and appears to migrate toward the center of the bone as the epiphyseal region grows away from it. The inner boundary of the lesion often is demarcated by a thin or prominent scalloped line of sclerosis Trabeculae frequently appear to traverse the defect and give it a multilocular appearance these trabeculae are, however, nearly always incomplete and the appearance is actually produced by the shadows of corrugations on the inner surface of the cavity housing the tumor Sometimes a fibroma has a poorly delimited periphery with no surrounding sclerosis. In thin bones the entire width of the bone may be involved. Central lesions may simulate fibrous dysplasia or simple bone cysts.



Fig. 10-2. Nonosteogenic fibroma of the left seventh rib of a 23-year-old woman. This lesion was asymptomatic and was discovered accidentally during routine roentgenographic study of the thorax.



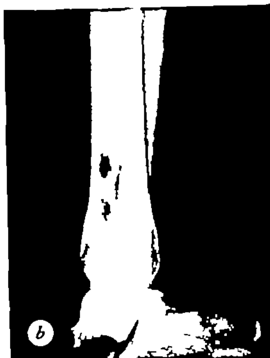


FIG. 10-3 *a*. Fibroma of the distal part of the tibia with classic features except for somewhat more than usual sclerosis. *b*. Lateral view of the same lesion.



FIG. 10-4. Another typical fibroma, although small. This one was found incidentally on roentgenographic study of the ankle of an 8-year-old girl



FIG. 10-5. This lesion was found incidentally in a 57-year-old man. It consisted of dense fibrous tissue with a sclerosed border and represented perhaps the late phase of a typical fibroma.

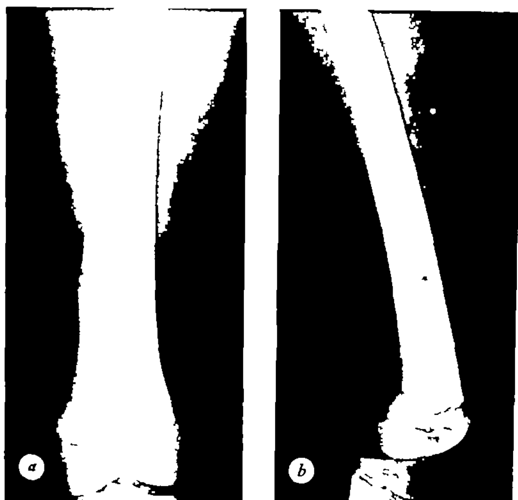


FIG 10-6 An unusually large fibroma in an 11-year-old girl. Its roentgenologic features, including an appearance of trabeculation, bulging of the cortical outline and a distinct inner boundary are typical. *b* Lateral view of the same lesion makes it appear to be basically central one. (Roentgenograms of this case were provided through the courtesy of Drs. P K. Odland, G L. Thomas and M B. Llewellyn, of Janesville, Wisconsin)

Gross Pathology

As indicated by the roentgenogram, the cortex is ordinarily intact over a fibroma unless fracture has occurred The lesions vary in greatest diameter some reaching 5 cm. or more The long axis of a lesion tends to parallel that of the affected bone. The tumor tissue itself is usually distinctly demarcated from the surrounding bone and consists of curetted fragments of more or less fibrous, fleshy tissue. It is often completely or partially yellow depending on its lipid content. Occasionally the tissue contains enough hemosiderin to make it distinctly brown The attenuated cortex may be virtually absent over the lesion.



METRIC 1

Fig. 10. Material removed by curettage from a large fibroma of the lower part of the tibia. The lighter zones represent the foci with many foam cells. The gross appearance is, on the whole, not diagnostic.

Histopathology

Microscopic examination reveals a dominant, cellular fibroblastic connective-tissue background. This characteristic allows differentiation from genuine giant cell tumors which, in sections from diagnostic portions, are not fibrogenic. Benign multinucleated cells, containing less nuclei on the average than those of giant cell tumor are irregularly distributed throughout the lesion. Nests of lipophages are often seen. They rarely dominate or even form a prominent part of the picture but one encounters an occasional lesion in bone that consists almost exclusively of similar foam cells and that might plausibly be regarded as a fibroma with extreme lipidization. Giant cells are uncommon in the foci of foam cells. Hemosiderin pigmentation of variable degree may be seen in some of the fibroblasts.

Occasional fibromas are active enough that mitotic figures may be found with comparative ease. The benign quality of the nuclei should allay the fear that one is dealing with a malignant tumor in such cases.

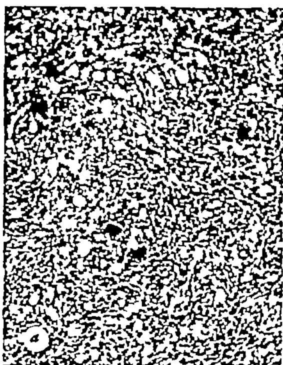




FIG. 10-8 *a.* Essential features of a fibroma, including fibroblastic connective tissue and benign giant cells. In addition, there are foam cells scattered throughout (×110). *b.* Prominent nests of foam cells in a fibroblastic stroma (×200)

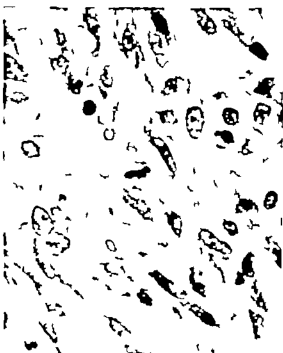


FIG. 10-9 Some fibromas, such as this one, exhibit worrisome cellularity, as evidenced by occasional mitotic figures (×400)



FIG. 10-10 Rarely, fibromas produce foci of osteoid, as at lower right, even without previous fracture (×210)

Treatment

If one is confident of the roentgenologic diagnosis and the structural integrity of the bone is not in question no treatment need be employed, and the progress of the lesion can be followed by repeat roentgenograms. Frequently the diagnosis is uncertain and then one can accomplish diagnosis and therapy with one surgical procedure. This tumor is readily eradicated by conservative surgical means, curettage ordinarily being employed. Bone grafting of the defect may be desirable if the lesion is large. Radiation therapy is contraindicated for two reasons, namely the inherent sarcoma producing potential of this form of therapy and the frequent proximity of the fibroma to a growing epiphyseal line

Prognosis

As indicated, conservative surgical treatment, when necessary is curative. Many lesions have been shown to undergo spontaneous regression. It has been observed that fracture through one of these lesions heals but the defect in the bone usually persists.

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Chapter 11

Hemangioma, Hemangioendothelioma and Hemangiopericytoma

In a consideration of neoplasms primarily in bone that require surgical procedures for diagnosis or therapy tumors of vascular origin play a minor role Although evidence of hemangiomas is seen fairly often in roentgenograms of the vertebrae and skull, their relative scarcity among surgical specimens indicates that many of these are merely asymptomatic incidental findings. Certainly if one excludes the skull and vertebrae, hemangioma becomes a distinct rarity among the defects seen in bones. Despite this rarity multiple bones are sometimes involved This discussion excludes those cases of diffuse hemangiomatosis of an extremity in which bone may become distorted with or without actual involvement by the vascular process.

Hemangioendotheliomas (angiosarcomas) of bone are very uncommon, a review of the world's literature in 1956 yielding only 16 examples.

Hemangiopericytomas, including the well-differentiated glomus tumors, have been seen in bone.

The rare and bizarre condition called "phantom" or "disappearing" bone disease has recently been related to hemangiomatosis of the affected sites.

Representative examples of vascular tumors in bone appear on the following pages but their nonspecific clinical features and their standard pathologic characteristics will not be discussed.

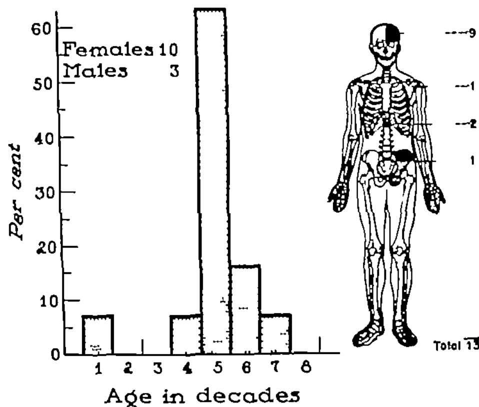


FIG. 11 1 Skeletal, age and sex distribution of hemangiomas alone.

Incidence

The 13 hemangiomas in the present series comprised only 0 6 per cent of the total tumors. In addition the series included three malignant blood vascular tumors (hemangioendotheliomas) and two hemangiopericytomas

Sex

Although females predominated in this series the literature indicates no distinct predilection for either sex

Age

The peak incidence in the fifth decade, shown in the illustration above, is probably not of statistical significance. According to most reports, hemangiomas affect adults of all ages

Localization

At least two thirds of surgically explored hemangiomas are found in the skull and vertebrae The relative predilection for these bones increases if one includes all cases in which evidence of such lesions is seen in roentgenograms.





FIG. 11 2 (*above*) Characteristic, fairly sharply delimited defect produced by a cavernous hemangioma of the skull. Although a sunburst appearance has been attributed to hemangiomas that have expanded bones, such an [illegible] appearance has been unusual in the experience of the Mayo Clinic.

FIG. 11 3 (*left*) Rarefaction of the vertebral body with exaggerated vertical striation, changes commonly attributed to hemangioma in this location. (Reproduced with permission from Pugh, D. G *Roentgenologic Diagnosis of Diseases of Bone* Baltimore, Williams & Wilkins, 1954, *pp 559AS-559AV*)



FIG. 11-4. Cavernous hemangioma of the skull. Thin-walled large blood vessels are interspersed among the osseous trabeculae (×95). This is the same case as that represented in Figure 11-2.



FIG. 11-5. Hemangiopericytoma that had expanded the ascending ramus of the mandible. The intervascular portions were characterized by varying degrees of cellularity (×200).



FIG. 11-6. Hemangioendothelioma (angiosarcoma) that had caused destruction of the second lumbar vertebra of a 38-year-old man (×360).



Fig. 11.7 "Phantom" or "disappearing" bone disease. The female patient whose roentgenogram is shown above had difficulties that began with pathologic fracture of a rib 5 years before this picture was taken. Eight years after onset, having lost all or part of most of her right ribs and the ninth, tenth and eleventh thoracic vertebrae she succumbed to the effects of this destruction of her thoracic cage



Fig. 11.8 The vascularity of the specimen procured for biopsy from one of the affected ribs shown in the roentgenogram in Figure 11 is sufficiently prominent to support the diagnosis of hemangioma (×65)

Treatment

Local curettage therapy is indicated for well-circumscribed benign cases. Extensive benign vascular tumors are sometimes treated by irradiation. When possible, frankly malignant vascular tumors should be treated by amputation or at least, by radical local excision.

Prognosis

Most localized hemangiomas respond satisfactorily to conservative measures. The frequent development of metastasis to other bones and to the lungs in the case of hemangioendothelioma (angiosarcoma) dictates the necessity for radical early treatment.

Chapter 12

Lipoma and Liposarcoma

Despite the abundance of adipose connective tissue in bone marrow, lipomas of bone are extremely rare. Child in 1955 described one involving the os calcis and found only three intraosseous lipomas reported in the literature. Lipomas of soft tissues adjacent to bone, sometimes even apparently arising in or under the periosteum, may cause erosion of bone but such is rare. Discrete, small collections of adipose connective tissue that might possibly be considered neoplastic are sometimes seen in vertebrae.

Liposarcoma of bone can occur as evidenced by the case described by Dawson in 1955. She found that several of the eight cases she collected from the literature were difficult to accept. No unequivocal liposarcoma of bone was found in the present series. Tumors containing the large, sometimes vacuolated, pleomorphic cells that make one think of liposarcoma have been included among the osteogenic sarcomas in this series. This was done because foci of similar pleomorphic cells occur in some tumors that are obviously osteogenic sarcomas.



FIG. 12 1 Lipoma of the ulna of a 44-year-old man who had had a lump in the region of involvement for 30 years. He had no complaints referable to the lesion. The roentgenologist interpreted the process as probably neoplastic and suggested the possibility of its being malignant. (Reproduced with permission from Caruolo, J E. and Dahlin, D C. *Proc Staff Meet Mayo Clin* 28.361 363 1953)



FIG. 12 2. Lipoma excised from the region of involvement shown in Figure 12 1 The tumor was found beneath the periosteum and it had produced irregular partially localized erosion of the cortex.



FIG. 1-3. Lipoma involving the left frontal bone of a 31-year-old man. This lesion, which measured 1.5 by 1.5 by 0.4 cm. when excised, was apparently an incidental finding on a roentgenogram taken because of the patient's complaint of headache of 2 years' duration.

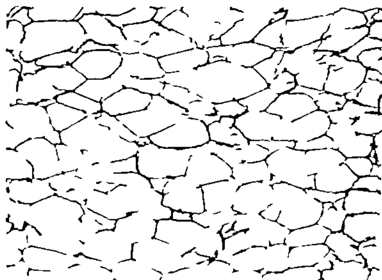


FIG. 1-4. Typical histologic appearance of lipoma. This picture is representative of the tissue seen in the case shown in the roentgenogram above and in the one on the preceding page (×120).

Treatment

Treatment of the rare lipoma one may encounter in bone should be conservative The necessity for surgical intervention is ordinarily dictated by failure to make a correct preoperative diagnosis

The available evidence indicates that prompt ablative surgical treatment is the one of choice for liposarcoma.

Prognosis

Conservative therapy should, obviously be curative in the case of lipomas.

Liposarcomas may produce death from metastasis even after prompt treatment by radical surgical means.

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Chapter 13

Neurilemmoma and Related Tumors

NEUROGENIC TUMORS arising in bone are rare. A few bona fide neurilemmomas that obviously arose in bone have been described. More often one sees secondary bony changes due to erosion by a neurilemmoma of soft tissue origin, especially along the spinal column or in the cranium.

Neurofibromatosis has been found to be associated with a variety of skeletal changes including scoliosis, subperiosteal bone cysts, skeletal hypertrophy absence of the posterior wall of the orbit, and congenital pseudarthrosis. Unfortunately many of the skeletal defects that have been seen in von Recklinghausen's neurofibromatosis have been studied only roentgenologically and their exact pathologic nature is obscure. Since histologic examination of neoplasms often affords inadequate evidence to prove or disprove their neurogenic origin, some of the conclusions derived from studies of tissue are, likewise, subject to criticism.

Malignant tumors of neurogenic origin have rarely been described as arising in bone. The inherent characteristics of a malignant growth make it doubly difficult to verify the exact tissue of origin in a questionable case.





Fig. 13-1 Neurilemmoma of the mandible. *a*. Tissue section (×180) *b* An expanding lesion is evident. This neurilemmoma was found in a 64-year-old woman and the clinical history suggested that it had been present for 20 years.

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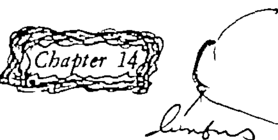
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Myeloma

THIS TUMOR of hematopoietic derivation is the most common neoplasm of bone, in the experience of my colleagues and me. It is composed of plasma cells showing variable degrees of differentiation. The neoplastic process is usually multicentric and often involves the bone marrow so diffusely that it may be diagnosed in the great majority of cases by marrow aspiration.

Myeloma, especially in the disseminated form, produces metabolic disturbances which account for the common appearance of hyperglobulinemia (sometimes including cryoglobulins and pyroglobulins) hypercalcemia, Bence Jones proteinuria, rapid sedimentation rate, rouleau formation of erythrocytes, and renal dysfunction due to protein casts in the tubules.

Electrophoretic and physical studies have diagnostic value and are increasing the knowledge of the deranged metabolism. Amyloidosis occurs in about 10 per cent of patients it may be systemic or appear only as large or minute masses in the neoplastic tissue or elsewhere.

Myeloma cells are found not uncommonly in small numbers in peripheral blood in rare cases a leukemic blood picture is produced. Anemia often results from the replacement of bone marrow

"Solitary" Myeloma

Occasionally one sees a single osseous focus of myeloma which is associated with normal sternal marrow and with few or none of the systemic derangements indicated above These cases almost invariably develop into cases of disseminated myeloma, but sometimes only after a latent period of 5 to 10 years or even longer A morphologic counterpart of "solitary" myeloma occurs primarily in soft tissues and has a better prognosis

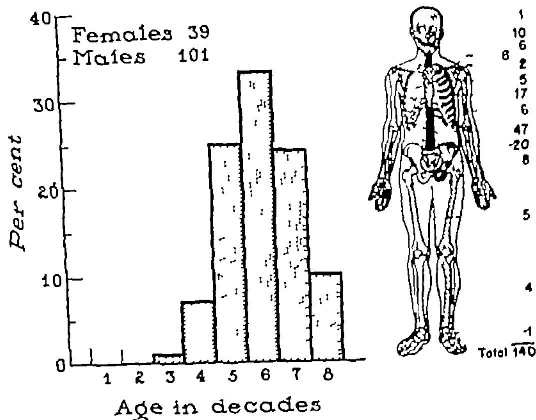


FIG. 14-1 Skeletal age and sex distribution of 140 surgical cases.

Incidence

The total of 563 cases of myeloma constituted 34 per cent of the malignant bone tumors in this series

Sex

In most recorded series males have comprised from 60 to 75 per cent of cases

Age

The graph above accents the well-known rarity of myeloma before the fifth decade of life

Localization

As one might expect, the bones that contain hematopoietic marrow in adults harbor most of the recognizable myeloma nodules. Although the data tabulated above are selected since they are based on the 140 surgical cases only the distribution shown is similar to that observed at necropsy except that the skull is almost always involved in an unselected series by the time myeloma has caused the patient's death. Initially "solitary" myelomas have a skeletal distribution much like that of the disseminated form. Lymph nodes, liver and spleen commonly and other soft-tissue organs sometimes, are involved in disseminated myeloma of bones

Symptoms

Pain of an increasing nature is the most common complaint of patients with myeloma, and it is most often centered in the lumbar or thoracic spinal regions. On the average, the pain is of less than 6 months' duration prior to the time the patient is admitted, but sometimes it has been present for several years. Weakness and loss of weight occur during the course of the disease in nearly every case of myeloma. Pathologic fracture, with abrupt onset of symptoms, is common and the majority of such fractures involve the vertebral column. Neurologic symptoms, usually from involvement of the spinal cord or nerve roots secondary to pathologic fracture or extraosseous extension of the neoplastic tissue, are frequently observed. Complaints referable to renal involvement may be encountered. Less common symptoms include palpable tumor, hemorrhagic tendency, anemia and fever.

Physical and Laboratory Findings

The physical findings are generally nonspecific. Local pain or tenderness, with or without palpable tumor, is sometimes elicited. Evidences of neurologic dysfunction, pathologic fracture and anemia may be observed.

Laboratory studies are far more helpful in the diagnosis of disseminated myeloma than in the diagnosis of any other bone tumor. Smears of peripheral blood often show excessive rouleau formation and, more important, have been reported to contain myeloma cells in from 10 to 73 per cent of patients. The erythrocyte sedimentation rate is notoriously rapid. Anemia is common in patients with disseminated myeloma, owing to replacement of marrow by tumor. Hyperglobulinemia, often unassociated with hyperproteinemia, occurs in the majority of patients and cryoglobulins may be demonstrated in a few. Electrophoretic and physical studies aid in determining the presence and nature of the abnormal serum proteins. Hypercalcemia is commonly observed. Bence Jones protein is detected at some time in the urine of more than half the myeloma patients, and albuminuria is even more common. Evidences of renal insufficiency or amyloidosis, which may be generalized, sometimes develop. Levels of serum alkaline phosphatase are rarely elevated even in the face of widespread osseous lesions.

Roentgenologic Features

These features result from replacement of osseous structures by the myelomatous masses. The first and most extensive changes usually occur in the ribs, vertebrae, skull and pelvis. Classically there are "punched out" areas of bone destruction which vary up to 5 cm. in diameter and about which there is no surrounding zone of sclerosis. Expansion of the affected bone may produce a "ballooned-out" appearance, especially in the ribs. A [illegible]rable degree of osteoporosis is common, and pathologic fracture, especially of vertebrae, is often seen. From 12 to 25 per cent of patients with myeloma are reported to have no discernible foci of bone destruction. Some of these, on close scrutiny, will be found to have diffuse demineralization of portions of the skeleton. Metastatic carcinoma, reticulum cell sarcoma and hyperparathyroidism can produce bone lesions that simulate those of myeloma. "Solitary" myeloma lesions of bone are classically destructive but they too may produce expansion of the bone's contour.



FIG. 14-2. Myeloma in one of the most commonly affected sites. There are numerous discrete foci of osseous destruction.



FIG. 14-3. Another classic example of multiple myeloma. As in the preceding illustration, the discrete foci of rarefaction are not associated with sclerosis of bone. (Reproduced with permission from Pugh, D. G. *Roentgenologic Diagnosis of Diseases of Bone*. Baltimore: Williams & Wilkins, 1954, pp. 487-492.)



FIG. 14-4. *a* (*left*) Expansile lesion of the clavicle. This proved to be myeloma of the solitary type. A fracture, apparently pathologic, occurred through this region in September 1950, and again in January 1953. The clavicle was excised in April, 1953. When last heard from 2½ years later the patient was alive and well. *b* (*below*) Excised specimen from the case illustrated on the left.







FIG. 14-5. *a* (*above*) Destruction of humerus produced by solitary myeloma. Forequarter amputation was performed on November 11, 1955. Sixteen months later signs of dissemination were present. An erroneous diagnosis of reticulum cell sarcoma was made at the time of amputation. *b* (*left*) Gross specimen in the same case.

Gross Pathology

The myelomatous masses are classically soft, gray and friable, resembling the tissue of a malignant lymphoma. As with other invasive tumors, more marrow will be seen to be involved than is indicated by the roentgenologic changes. Expansion of the affected bone and, even more commonly extraosseous extension of the tumor contribute to damage to adjacent structures. Extraosseous lesions are sometimes grossly discernible in other portions of the hematopoietic system, notably in the lymph nodes and spleen. As indicated, pathologic fracture may be present and often results in damage to the spinal cord. In very rare instances enough amyloid is formed by the tumor to be grossly obvious.

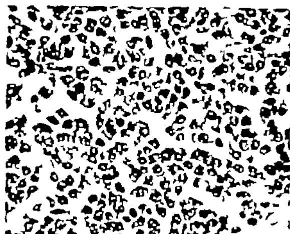
Histopathology

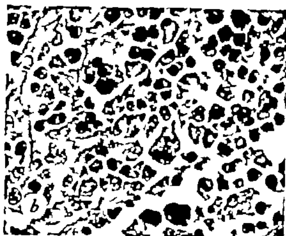
Typically one sees sheets of closely packed cells with little intercellular substance. These cells have abundant cytoplasm which tends to be granular and basophilic. The cell outlines are distinct and the nucleus is characteristically round or oval and eccentric. Two or even three nuclei are sometimes observed. When one studies a series of cases of myeloma, gradations are found to exist, these apparently reflecting the maturity or degree of differentiation of the cells. At one extreme are tumors with cells closely resembling the plasma cells seen in inflammatory conditions these show prominent clumping of chromatin, sometimes producing the "wheel-spoke" appearance. With decreasing differentiation, nucleoli become large and clumping of chromatin is less marked. Cytoplasmic vacuoles increase in prominence and the cell boundary becomes indistinct. Finally the nuclei may have grooves and lobules and at the other extreme is a tumor that may be indistinguishable from reticulum cell sarcoma. In fact some myelomas have foci that are quite like reticulum cell sarcoma and some even contain multinucleated cells of such size that the diagnosis of Hodgkin's sarcoma may be considered. The occasional shading together of these tumors should not be surprising since all three very likely are basically of reticuloendothelial derivation.

Mitotic figures are rare in the average myeloma. The similarity of the cells comprising the solid sheets in this tumor contrasts with the multiplicity of cell types in the occasional chronic inflammatory focus that superficially resembles myeloma. The inflammatory pseudoneoplasm often contains a prominent capillary network that aids in differentiation.

A variety of extraosseous manifestations of myeloma are important but a detailed consideration of them is beyond the scope of this discussion. The reader is referred to the excellent descriptions of these lesions by Carson, Ackerman and Maltby in 1955 and by Churg and Gordon in 1950.

Bayrd's article in 1948 describes the cytologic details of myeloma cells as seen in marrow smears.





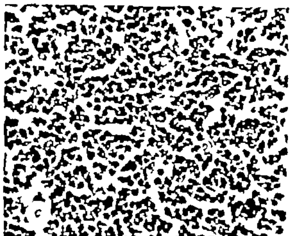








FIG. 11-6. *a*, Relatively well-differentiated myeloma with characteristic eccentric nuclei and abundant cytoplasm (×380). *b*, Highly malignant myeloma at the same magnification as in *a*. Note the large nuclei and the multinucleated giant cells (×380). *c*, Same tumor as that illustrated in *a* (×265). *d*, Wright-stained smear of sternal marrow containing typical myeloma cells (×850). *e*, Amyloid masses in a myeloma nodule. Note benign giant cell reaction commonly seen around amyloid masses (×135). *f*, Myeloma cells that contain amyloid or a precursor. This is an extremely rare finding (×800). (Figure 14-6 reproduced with permission from Dahlin, D. C. and Dockerty, M. B.: *Am. J. Path.* 26:581-595, 1950.)

Treatment

The mode of treatment in myeloma varies, depending upon whether the disease is solitary or disseminated.

For localized myeloma radiation is the treatment of choice. Excision (total if possible) or at least diagnostic biopsy should precede radiation. Aspiration biopsy has been used successfully in a number of Mayo Clinic patients with vertebral involvement. In the patients with severe neurologic symptoms, decompression of the spinal cord may be necessary prior to radiation. Therapy must be directed at preservation of the spinal cord since many patients with a "solitary" lesion may live several years before dissemination occurs.

Urethane or a combination of urethane and steroids is the mainstay of therapy in patients with disseminated myeloma. In addition to symptomatic relief there is probably some prolongation of life as a result of such treatment. If a patient continues to have pain due to a tumefaction after a few weeks of systemic therapy local radiation may be necessary. Other forms of systemic treatment, of as yet unproved additional value have been advocated.

Prognosis

The average patient with disseminated myeloma dies within 2 years after diagnosis, although some survive a much longer time. Inanition, anemia, involvement of the spinal cord, and renal failure are the major factors contributing to the death of these patients. As indicated, in nearly all cases of "solitary" myeloma the disease eventually disseminates.

Occasional patients die from the effects of a complicating systemic amyloidosis.

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Chapter 15

Reticulum Cell Sarcoma (Primary Malignant Lymphoma of Bone)

PRIOR TO THE CLASSIC ARTICLE by Parker and Jackson in 1939 reticulum cell sarcomas were generally "lumped" with Ewing's tumors. The remarkably good prognosis as well as clinical implications makes it important to recognize this special tumor. Perhaps more than any other sarcoma of bone it tends to involve regional nodes.

Study of an osseous lesion produced by malignant lymphoma will not disclose whether it is primary and localized or part of a disseminated process. Accordingly one must study the patient thoroughly before embarking upon a course of treatment. Osseous lesions are commonly seen in the later stages of any of the malignant lymphomas of soft-tissue origin and in leukemias. Although it is not surprising to have a localized lymphoma of bone eventuate in systemic disease, it is extremely unusual for early leukemia to masquerade as a primary tumor of bone.

Malignant lymphomas of the lymphocytic, reticulum cell and even Hodgkin's type are encountered as primary lesions of bone. The great predominance of the reticulum cell variety as well as the frequency with which reticulum cells occur in the other members of the group, has led to the general use of the term "reticulum cell sarcoma" for this category of tumors.

Tumors of this type are morphologically identical to their soft-tissue counterparts. It is not surprising that malignant lymphomas may be primary in bone when it is recalled that they begin in such structures as the spleen, stomach, small intestine and thyroid gland.

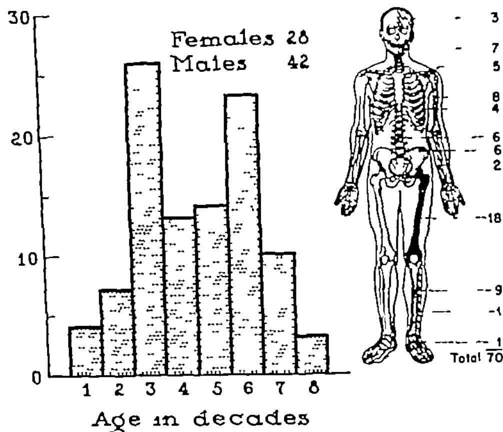


Fig. 15-1. Skeletal, age and sex distribution of reticulum cell sarcoma.

Incidence

Reticulum cell sarcoma comprised 4.2 per cent of the malignant group in this series. In a minority of the cases included, lesions were present in more than one bone, but the tumor apparently was primary in bone. The very rare lymphocytic lymphoma and Hodgkin's malignant lymphoma primary in bone have not been included in the present series.

Sex

Males predominate in a ratio of approximately 3 to 2.

Age

Recorded data show that this neoplasm can occur at any age but is rare in the very young.

Localization

When a malignant lymphoma arises in specific sites such as the antrum or along the spinal column it is often impossible to prove an osseous origin. The recorded data are therefore, weighted against these locations. A tumor of this type, when in a long bone, is often extensive and may involve any portion of the bone. In this series, two involved the ulna, three the skull, seven the mandible, five the scapula, one each the fibula and tarsal bones, and four the ribs.

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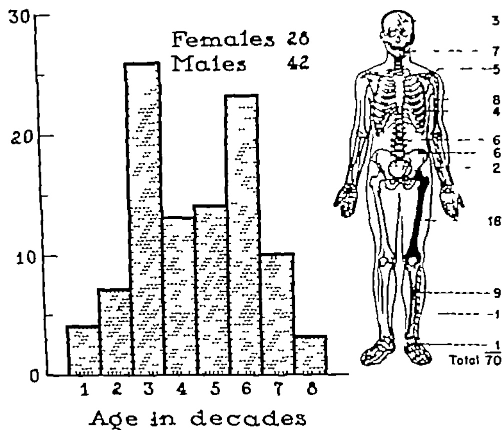


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Symptoms

Pain, swelling and subsequent disability are the cardinal features of any malignant tumor of bone, including reticulum cell sarcoma. Pain of variable intensity is practically a constant feature, and occasionally it has been present for several years, although ordinarily its duration is measured in months. Neurologic symptoms commonly occur when these tumors affect the spinal column. Many have emphasized that patients with even extensive solitary malignant lymphomas have a surprising sense of well being and absence of general complaints so commonly associated with malignant disease. Pathologic fracture may occur

Physical Findings

A mass in the region of the tumor which may be tender or warm, is the main finding, and this is often associated with disability of the affected part. Enlarged regional lymph nodes may be found. One should search for signs of disseminated malignant lymphoma, such as involvement of multiple bones, distant lymph nodes and other soft tissue structures. Because of the occasional similarity of tumefactions due to malignant lymphomas and those due to leukemia, it is important to study the peripheral blood of these patients.

Roentgenologic Features

Roentgenologically the lesions frequently appear to be very extensive, often involving 25 to 50 per cent of the affected bone and in some cases involving the entire shaft. Bone destruction is the predominant feature of primary reticulum cell sarcoma The areas of destruction give the bone a mottled and patchy appearance in many cases and sometimes its outline is entirely lost The diseased bone blends imperceptibly with the adjacent normal bone. Approximately half the patients in this series have shown evidence of some reactive proliferation of new bone that is not laid down by the tumor cells themselves. Nearly every malignant lymphoma produces destruction of cortical bone, and approximately 25 per cent are associated with some thickening of the cortex. There is often obvious soft-tissue extension of the tumors and sometimes there is calcification in the soft-tissue mass. In approximately one fourth of the cases there is evidence of pathologic fracture

Irregular sclerosis of the affected site is sometimes a marked feature and adds to the confusion of reticulum cell sarcoma with chronic osteomyelitis that sometimes occurs. Disseminated malignant lymphomatous involvement of the skeleton may simulate osteoblastic metastatic carcinomatosis.

Wilson and Pugh, who studied the Mayo Clinic series, concluded that the roentgenograms varied so much that their appearance could not be regarded as characteristic Although the radiologist can frequently suspect the diagnosis of reticulum cell sarcoma, other lesions including osteogenic sarcoma, Ewing's tumor eosinophilic granuloma and chronic osteomyelitis cannot always be excluded with certainty

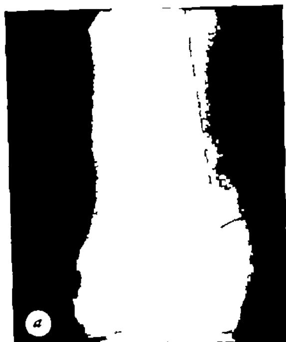




Fig. 15-2. Anteroposterior (*a*) and lateral (*b*) views of primary malignant lymphoma destroying the lower portion of the femur. There is blotchy sclerosis in the area of destruction. (Figure 15-2a reproduced with permission from Ivins, J. C. and Dahlin, D. C.: *J. Bone & Joint Surg.*, 35A:835-842, 1953.)



Fig. 15-3 (*right*). Typical destruction produced by one of these tumors. Note that the lesion is extensive, has disrupted the cortex, has resulted in zones of sclerosis and subperiosteal new bone, and has a large soft-tissue component. Despite *roentgen therapy, which was unsuccessful, and* forequarter amputation this tumor resulted in death of the patient less than 2 years after the onset of symptoms.

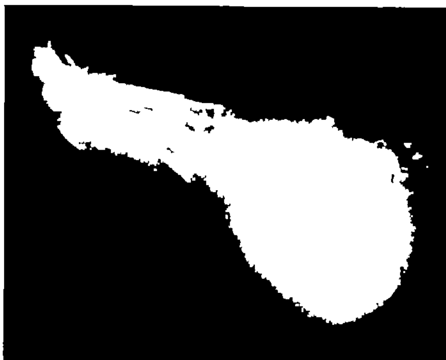




FIG. 15-4 (*above*) Reticulum cell sarcoma producing marked destruction of the tarsal bones of a 65-year-old woman. Inguinal nodes were enlarged and biopsy material from one of these presented the characteristic pattern of malignant lymphoma of the reticulum cell type.

FIG. 15-5 This reticulum cell sarcoma of the tibia occurred in 43-year-old man who had noted pain in the involved region for 5 years. The original interpretation of the roentgenograms was osteomyelitis involving the upper three fourths of the tibia. The sclerosis produced by this tumor is like that sometimes seen in the skeletal lesions produced by any of the malignant lymphomas.



FIG. 15-6. Reticulum cell sarcoma of the distal part of the femur of a 38-year-old man. A previous biopsy had disclosed what was called an "inflammatory" lesion, and at the time of amputation the tumor had grown through the skin. (Reproduced with permission from McCormack, L. J., Ivins, J. C., Dahlin, D. C. and Johnson, E. W., Jr.: *Cancer* 5:1182-1192, 1952.)

Gross Pathology

The gross features of primary malignant lymphoma of bone are not pathognomonic, but some of them warrant mention. Although any portion, and frequently a large part of a long bone may be involved, the extraosseous tumefactive extension is often near or at the end of the shaft. A variable amount of soft tissue extension is practically always present by the time diagnosis is made. The bone itself at the affected site is destroyed to a variable extent, and not infrequently one sees white areas of necrosis which sometimes show calcification. Residual osseous trabeculae are frequently admixed with tumor, imparting a firm and gritty consistency. When a reticulum cell sarcoma extends into the soft tissues it produces a soft mass that is friable and simulates the appearance of malignant lymphomas arising in soft tissues. The

margins of a malignant lymphoma in the bone as well as in the adjacent soft tissues are ordinarily indistinct. Regional lymph nodes may be involved and, as indicated above, there may be any of the gross pathologic evidence of disseminated malignant lymphoma.



FIG. 15-7 Primary malignant lymphoma (reticulum cell type) involving practically the entire length of the tibia even though there is very little extension into the soft tissue. Pathologic fracture had occurred.

Histopathology

The basic proliferating cell in tumors of this type is the reticulum cell. It characteristically has a grooved or folded nucleus, one or more distinct nucleoli, and indistinct, irregular cytoplasmic boundaries. Cytoplasmic processes may extend outward from the cell bodies. A large proportion of these tumors contain variable numbers of lymphoblasts and lymphocytes, and sometimes these cells dominate the histologic picture. On rare occasions one encounters a pure lymphocytic malignant lymphoma that is apparently primary in bone. Occasional highly malignant reticulum cell sarcomas of bone contain multinucleated cells of the Reed-Sternberg type, and these tumors quite logically fall into the category of Hodgkin's sarcoma

Since the cells of the average malignant lymphoma lie in a reticular framework there is a tendency for an alveolar grouping, a feature which is often prominent even under low magnification. This helps differentiate reticulum cell sarcoma from Ewing's tumor in which large masses of cells are associated with no fibrillar intercellular material. Special stains for reticulum accentuate the network in which the cells lie In my experience, however this stain has been of little value for diagnosis because those tumors that appear atypical when stained with ordinary dyes contain an equivocal amount of stainable reticulum. There is no discernible difference between malignant lymphoma that begins in bone and malignant lymphoma that begins elsewhere in the body

As noted by Parker and Jackson, the large numbers of lymphocytic cells present in some of these tumors may lead to the diagnosis of an inflammatory process, an error especially likely to occur if one has only a small amount of material for biopsy As indicated, a large number of these neoplasms contain

a variably small to great proportion of lymphocytes. The microscopic counterpart of the lack of gross encapsulation of these tumors is an irregular invasion of adjacent tissues by the neoplastic cells

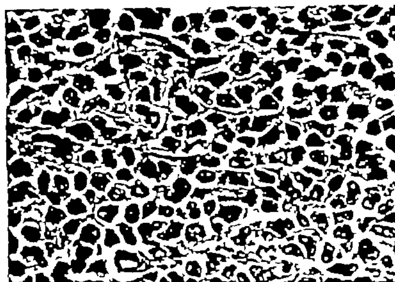


FIG. 15-8. Classic reticulum cell sarcoma with cells showing grooved and indented nuclei, indistinct cytoplasmic borders, and a reticular framework that is easily seen even with this hematoxylin and eosin stain (×650)



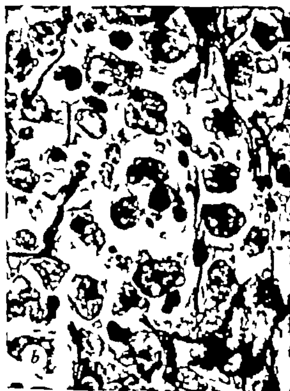
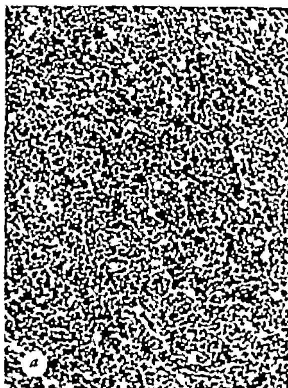


FIG. 15-9. *a.* Characteristic alveolar pattern of reticulum cell sarcoma, in this instance invading and destroying trabeculae of normal bone (×125). *b.* Higher magnification to show nuclear detail and strands of reticulin (reticulin stain ×800) (Reproduced with permission from Ivins, J. C. and Dahlin, D. C. *J. Bone & Joint Surg.* 35A:835-842, 1953.)



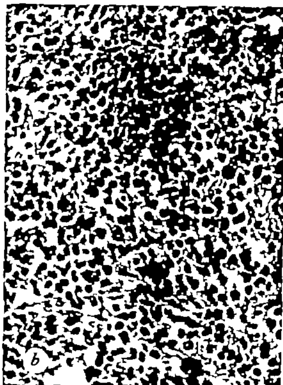


Fig. 15-10 *a*, Typical alveolar pattern of reticulum cell sarcoma. Even at this magnification the reticular framework is visible (×115). *b*, In this field are seen lymphoblasts and lymphocytes, cells commonly found in malignant lymphomas primary in bone (×300).

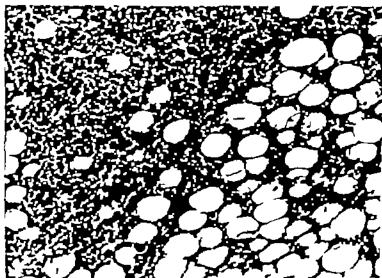


Fig. 15-11 Reticulum cell sarcoma with invasion into the adjacent fat. tes are that accounts for the poorly defined border ordinarily seen on gross inspection of one of these lesions (×150). (Reproduced with permission from McCormack, L. J., Ivins, J. C., Dahlin, D. C. and Johnson, E. W., Jr. Cancer 5 1182-1192, 1952.)

Treatment

The accumulated experience with primary malignant lymphomas that are apparently solitary in bone does not yet allow one to be dogmatic regarding the treatment of choice. The consensus now apparently favors irradiation for control of the primary lesion. Sometimes curative irradiation results in local necrosis that is disabling and sometimes it fails to halt the growth of the primary tumor These facts have made some feel that primary ablative surgical procedures should be used whenever possible. It is clear that the regional lymph nodes require attention, and radiation therapy is likely most efficacious for these Irradiation is certainly indicated for those tumors not amenable to surgical removal.

Prognosis

Most reports indicate that reticulum cell sarcoma has the best prognosis of any of the primary malignant tumors of bone. A 5-year survival rate of 40 to 50 per cent can be expected for patients that are adequately treated and in whom there is reasonable evidence that the lesion is localized. No rule applies, however to an individual case, because of the well-known vagaries of the malignant lymphomas. Patients with one lesion adequately treated may have, in a period of months or many years, a tumor in another bone, in a distant lymph node or in other soft tissue, or they subsequently may even have a leukemic blood picture.

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Chapter 16

Primary Chondrosarcoma

CHONDROSARCOMA should be separated from osteogenic sarcoma because of basic pathologic differences which are reflected in vastly differing clinical, therapeutic and prognostic features. The exact origin of chondrosarcomas is obscure but the salient pathologic fact is that their basic proliferating tissue is cartilaginous throughout. Large portions of these tumors may become myxomatous, or calcified or even ossified. Sometimes fibrosarcomalike spindling of the cells is seen at the peripheries of the lobules of the tumor. Osseous trabeculae, when present, result from differentiation of chondroid substance. When, however, the malignant cells produce an osteoid lacework or osteoid trabeculae directly even in small foci, the neoplasm has the clinical characteristics of osteogenic sarcoma and belongs in that category.

Chondrosarcoma usually has a slow clinical evolution. Metastasis is relatively rare and often late in appearance. Therefore, unlike osteogenic sarcoma, in which prompt ablative surgical treatment is imperative because of early hematogenous dissemination, the basic therapeutic problem is prevention of recurrence by adequate control of the lesion locally. Attainment of this goal demands adequate, frequently radical, early surgical treatment.

Secondary Chondrosarcoma

Secondary chondrosarcomas most commonly arise in osteochondromas (osteocartilaginous exostoses) especially in the multiple, familial type. In my experience it is extremely unusual to have a chondrosarcoma develop from an enchondroma that was originally clearly benign on critical analysis. In the Mayo Clinic series of 19 secondary chondrosarcomas, 12 occurred in patients with multiple osteochondromas and seven arose in solitary osteochondromas.

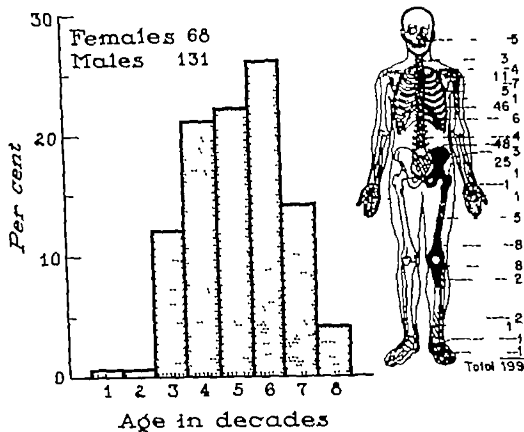


Fig. 16-1 Skeletal, age and sex distribution of primary chondrosarcoma.

Incidence

Chondrosarcoma constituted slightly more than 13 per cent of the malignant tumors in this series, and 90 per cent of these were of the primary type. Osteogenic sarcoma was more than twice as common.

Sex

The ratio of males to females was approximately 2 1

Age

The graph emphasizes that this tumor is one of adulthood and old age Significantly the second decade of life, in which the peak incidence of osteogenic sarcoma occurs, is practically immune to chondrosarcoma. The youngest patient in this series was 9 years old, and there was only one patient in the second decade.

Localization

Half of the tumors occurred in the pelvic girdle and ribs. More than three fourths were in the trunk (including the shoulder girdle) and the upper ends of the femora and humeri Thirteen arose from vertebrae, 11 from the scapula, four from the clavicle and five each from the maxilla and the sternum. The remarkable rarity of chondrosarcoma in the distal portions of the *extremities*, with only four of them occurring distal to the ankle and wrist joints, is noteworthy

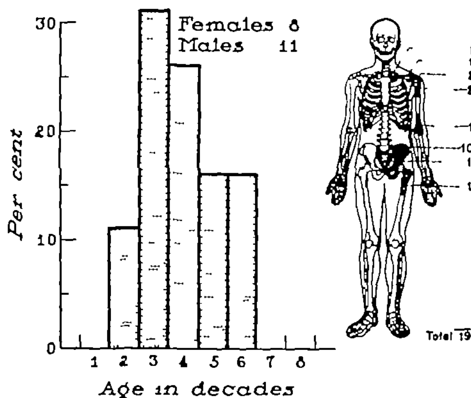


FIG. 16-2. Skeletal, age and sex distribution of secondary chondrosarcoma. Half of these tumors affected the innominate bone, but otherwise the sites of predilection are similar to those of primary chondrosarcoma. The sex and age distributions are also similar. There is a slight shift toward the younger age group which is perhaps explained by the origin of these sarcomas from what is likely a tumor due to congenital defect, namely osteochondroma. Apparently osteochondroma of the flat bones of the pelvis is especially prone to malignant transformation. None of the secondary chondrosarcomas in this series arose in a lesion of enchondromatosis.

Symptoms (All Chondrosarcomas)

Local swelling and pain, alone or in combination, are the significant presenting symptoms. Except for some of the tumors of the pelvic girdle or spinal column, where referred pain may precede local pain or discernible physical or roentgenographic findings, localization of these tumors is easy. As in other tumors of bone the characteristics of the pain or swelling offer little differential diagnostic aid. The prolonged clinical course so often observed affords a clue. A gradually enlarging tumor for periods ranging from one to two decades or even more may have been noted by those patients who have had an osteochondroma that undergoes malignant transformation. Such transformation often produces pain and rapid increase in size of a tumor of long duration. Patients with primary chondrosarcoma may also have had symptoms for several years before coming to definitive therapy. Inadequately treated tumors produce a typical history of many recurrences and, finally, of inoperable extension or metastasis that leads to death of the host. A few chondrosarcomas run a rapid clinical course because of a higher degree of malignancy initially or because of increased activity with recurrence.

The slow clinical evolution of chondrosarcoma is emphasized by the fact that approximately 10 per cent of those that produced recurrence in this series had intervals of from 5 to 10 years between treatment and

recurrence. Since recurrence may be so delayed, it is obvious that conclusions regarding efficacy of any form of treatment must be based not only on a sizable series of cases but also on such a series followed for a period of at least 10 years.

Physical Findings

Many chondrosarcomas produce a mass that can be palpated, but a sizable number of those affecting the trunk, or even the long bones of the extremities if they have not breached the cortex, will have pain alone to indicate the presence of a lesion. When a mass is palpable, it is characteristically hard and may be painful. When no mass can be palpated, the diagnosis may be difficult. This is especially true of those chondrosarcomas of the innominate bone that have not produced definite roentgenologic changes. The region of the acetabulum, where many of the chondrosarcomas originate, is notorious for such "hidden" malignant tumors

Roentgenologic Features

The roentgenogram is nearly always helpful and often affords almost pathognomonic evidence of chondrosarcoma. Osseous destruction in the lesional area combined with mottled densities owing to calcification and ossification are the usual findings. Central chondrosarcomas of long bones often produce fusiform expansion of the shaft associated with thickening of the cortex. Cortical destruction allows extraosseous extension of lesions that begin in the medulla. Those that do not involve the medullary cavity may show little or no cortical destruction but they usually contain minute or massive telltale calcific masses.

Chondrosarcoma of the innominate bone, especially near the acetabulum, may produce no discernible roentgenographic findings early. This is especially true of those that are completely lytic. Even large destructive lesions are quite nonspecific roentgenologically when they do not manifest mottling due to calcification or ossification.

The roentgenogram of an osteochondroma that has undergone malignant transformation may be similar to that of the benign lesion from which it originated, but the surface will ordinarily be indistinct and fuzzy and the clear demarcation from the adjacent soft tissue may be lost. A large mass, especially when associated with irregular shadows of bone or calcification, is especially characteristic. Sometimes the chondrosarcoma destroys and obscures the exostosis from which it arose. In the author's series, 12 of the 19 patients with secondary chondrosarcoma had multiple exostoses, and genesis of the malignant tumor from a benign osteochondroma could logically be assumed in these individuals even in the face of obscure evidence in the region of the chondrosarcoma



FIG. 16-3 Chondrosarcoma arising from an upper right rib of a 64-year-old man. His only symptom was local swelling of 1¼ years' duration.



FIG. 16-4 Heavily calcified chondrosarcoma of the innominate bone of [illegible]-year-old woman. This tumor had produced pain for 4 years. (Reproduced with permission from Dahlin, D. C. and Henderson, E. D. *J. Bone & Joint Surg.* *38A* 1025-1038, 1956.)



Fig. 16-5 Chondrosarcoma of the upper portion of the humerus of 70-year-old man He had had local pain and increasing swelling for 18 months.



Fig 16-6. Chondrosarcoma of the right innominate bone in a 36-year-old man who as is seen in the roentgenogram, had multiple osteochondromas.

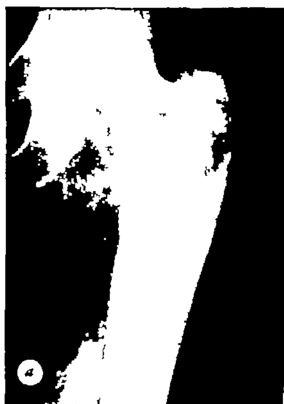




FIG. 16-7 *a.* Chondrosarcoma of the upper third of the femur. It has produced slight expansion of the shaft and thickening of the cortex. A small amount of calcification is present in the tumor. *b.* Another chondrosarcoma in this location. As can be seen from the roentgenogram, this tumor has broken through the cortex. The extraosseous mass had the pathologic features of grade 3 fibroblastic osteogenic sarcoma, although the intramedullary portion was typically grade 1 chondrosarcoma. (Fig. 16-7*a* reproduced with permission from Dahlin, D. C. and Henderson, E. D.: *J. Bone & Joint Surg.* 38A: 1025-1038, 1956.)

Gross Pathology

Chondrosarcomas may be divided into central and peripheral types. In the examples in long bones such a separation is usually obvious, with the rare peripheral sarcoma arising either on an osteochondroma or directly from the surface of a bone. In the case of thin or flat bones such as in the pelvic girdle or thoracic cage, landmarks are so destroyed by the time the average tumor comes to attention that the exact site of origin can only be surmised, but most of them apparently begin centrally. As seen in roentgenograms, central chondrosarcomas often produce expansion and concomitant thickening of the cortex of long bones. In such cases the region of involved marrow is distinctly demarcated. The thickened cortex is invaded by tumor and eventually break-through occurs.

These tumors are characteristically composed of lobules that vary from a few millimeters to several centimeters in diameter. Except at the tumor's periphery these lobules are more or less completely coalesced. The centers of the lobules often become necrotic, liquefied and cystic. Necrotic foci often calcify in an irregular fashion. Some of the calcific zones observed grossly are actually osseous masses.

Chondrosarcomas produce a matrix substance that varies in consistency from that of firm hyaline cartilage to that of mucus. Although there is little correlation between the degree of malignancy and the consistency of cartilaginous tumors, most of the myxoid ones are malignant. Sometimes the periphery or the recurrent form of a cartilaginous tumor is opaque and fibrous, resembling a fibrosarcoma or even an osteogenic sarcoma grossly and microscopically.

Metastasis to regional nodes is distinctly rare. Hematogenous dissemination to the lungs and elsewhere is uncommon when one compares chondrosarcoma to osteogenic or fibrosarcoma.

Chondrosarcoma has a marked propensity for local recurrence even when the surgeon "has gotten well around" the tumor.

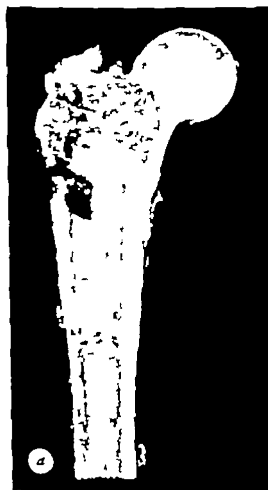




FIG. 16-8. *a* Gross specimen of the case illustrated in Figure 16-7*a*. Note the rather sharply defined margins of this tumor which extends into the femoral neck and has produced thickening of the expanded cortex, especially on the medial side. *b* Chondrosarcoma of the midfemur that has broken out into the periosseous tissues after having produced expansion of the bone and thickening of the cortex. (Reproduced with permission from Dahlin, D. C. and Henderson, E. D. *J. Bone & Joint Surg.* 38A 1025-1038, 1956.)



FIG. 16-9 Recurrent chondrosarcomatous implant in the peritoneal cavity. The primary tumor involved the right ilium. Note the lobulation, cyst formation and extensive central zone of necrosis. The scale in the right lower corner of the picture is 15 cm. long.



FIG. 16-10. Chondrosarcoma of the thoracic cage. This is the tumor illustrated in the roentgenogram in Figure 16-3.

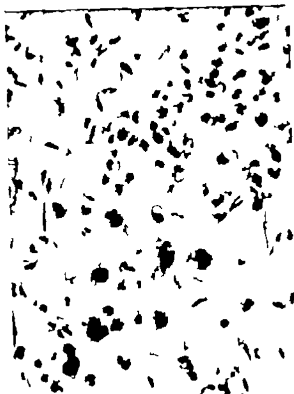


FIG. 16-13 Zone of grade 3 chondrosarcoma. Here the nuclear abnormalities and mitotic activity make the diagnosis *of sarcoma an obvious one* (×195)



FIG. 16-14. Chondrosarcoma, grade 1. Fair numbers of binucleated cells are present and the ground substance is *myxomatous.* The cartilage is differentiating into mature bone (×180)



FIG. 16-15 Grade 3 fibroblastic osteogenic sarcoma (×160) This highly malignant tumor developed in the scar after amputation for a grade 2 *chondrosarcoma that had fibrosarcomalike* elements at the periphery of the chondroid lobules. (Reproduced with permission from. Dahlin, D C. and Henderson, E. D *J Bone & Joint Surg 38A* 1025-1038, 1956.)



FIG. 16-16. Myxomatous grade 2 chondrosarcoma (×200). This is from a pulmonary nodule removed by segmental excision 16 months after a leg had been amputated for the primary tumor. The patient was alive and well 5 years after the excision of the metastatic nodule.

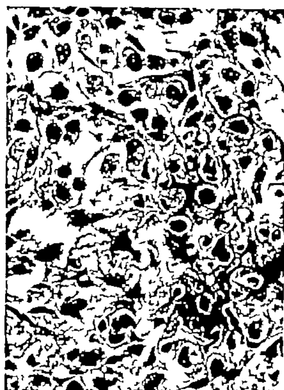


FIG. 16-17. Recurrent tumor shown in Figure 16-11 1 year after curettage of grade 1 chondrosarcoma. This recurrent lesion has features of osteogenic sarcoma, grade 2, as shown here (×300). Pulmonary metastasis became evident in less than year after amputation for this recurrent lesion.

Treatment

Surgery is the mainstay in therapy of this radioresistant tumor. Irradiation will serve, at best, as palliation for those tumors not amenable to surgical removal. Surgeons with wide experience in the treatment of bone tumors have learned that the optimal treatment for chondrosarcoma is early radical removal with as wide a margin of uninvolved tissue as possible. Certain of these tumors in the region of the iliac crests can be radically excised with preservation of the lower extremity. Most chondrosarcomas that involve the innominate bone or the upper end of the femur require hindquarter amputation for adequate removal. Those that are in the thoracic cage should be excised widely with an adequate margin of uninvolved tissue. Chondrosarcoma of the clavicle or scapula can often be treated by wide local removal, but a similar tumor in the upper end of the humerus is probably best treated by forequarter amputation. For those chondrosarcomas of the major tubular bones that are away from the trunk, wide local excision with bone grafting as necessary is sometimes feasible. In such instances, recurrent tumors are often amenable to more radical treatment.

Ideally, as with any of the surgical malignant tumors of bone, the definitive treatment should be carried out at the time of biopsy. First an adequate biopsy specimen must be obtained, one that allows the pathol-

ogist opportunity to make an accurate diagnosis The surgical team that performs the biopsy should change gowns, gloves and surgical instruments and redrape the patient. The definitive operation that is then performed should include the biopsy wound as part of the tissue to be completely removed or ablated because of the notorious capability of chondrosarcomas to produce recurrence by implantation The tumor itself should be completely excised with an adequate zone of surrounding tissue so that the surgeon does not break into or see the tumor at any time

Excision of secondary deposits that appear after the primary lesion has been controlled is sometimes worth while, as indicated by the case illustrated in Figure 16-16.

Prognosis

The fact that recurrences of chondrosarcoma are not uncommon after 5 years and sometimes are encountered even after 10 years makes it obvious that 5-year survival is not very significant as a criterion of cure. Actually because of the common error of underdiagnosis in the earlier part of the present series, the over all rate of cure for chondrosarcoma is less than for osteogenic sarcoma. Thoracic surgeons learned more than three decades ago that wide local excision was mandatory if one were to expect cure in the treatment of malignant cartilaginous tumors in the thoracic cage. Accordingly many of the long-term survivors in the Mayo Clinic series are patients who had chondrosarcoma in this location. But in the last 15 years, when hindquarter amputation has become common therapy for tumors in the pelvic girdle and upper part of the femur an increasing number of patients with chondrosarcoma in these locations are being cured. O'Neal and Ackerman have reported the rate for 5-year cure as 21 per cent.

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Chapter 17

Osteogenic Sarcoma

To QUALIFY in this category the proliferating malignant cells of the neoplasm must produce osteoid substance or material histologically indistinguishable from it in at least small foci A qualifying tumor, when sampled throughout, may show a predominance of elements with osteoid, chondroid or fibromatoid differentiation Accordingly this series of osteogenic sarcomas is divided into osteoblastic, chondroblastic and fibroblastic subtypes, depending on the dominating element. This subclassification may be confusing until one realizes that its function is merely to indicate that wide variation is seen in the histopathology of osteogenic sarcoma. All of these tumors, however have similar characteristics as regards bones of predilection, age of affected patients, marked tendency to early hematogenous dissemination and necessity for prompt ablative surgical therapy

It has not seemed practical to divide the osteogenic sarcomas into a variety of gross subtypes as has been done in the past. Whether the tumor is periosteal, sclerotic, lytic, central," telangiectatic and so forth makes little difference if it is a bona fide osteogenic sarcoma.

Although the great majority of these tumors are of unknown cause, more than 100 have been reported as a complication of Paget's disease and an increasing number of sarcomas following in the wake of radiation therapy to bone are being recorded.

A special type of osteogenic sarcoma which grows slowly metastasizes late if at all, and is characteristically juxtacortical or parosteal in location is known as parosteal osteogenic sarcoma. This is discussed in the next chapter

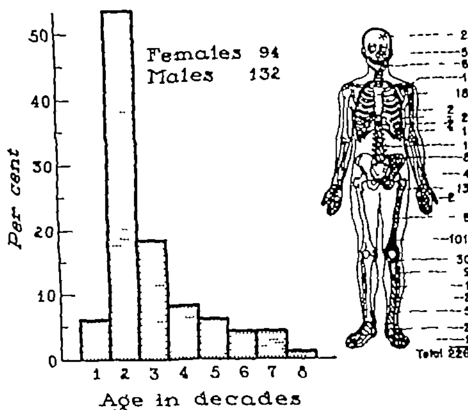


Fig. 17 1 Skeletal age and sex distribution of osteoblastic osteogenic sarcoma.

Incidence

The 469 osteogenic sarcomas (excluding the parosteal variety) comprised 28 6 per cent of the total sarcomas in this series, and 48 2 per cent of the osteogenic sarcomas were of the osteoblastic type.

Sex

Sixty-two per cent of all the patients with osteogenic sarcoma were males.

Age

Although there are a few osteogenic sarcomas in the first decade of life the peak incidence is in the second decade and there is a steady gradual decrease thereafter The youngest of 469 patients with osteogenic sarcoma was 4½ years old

Localization

The metaphyseal part of the long bones is the site of predilection, and the region of the knee accounted for half of the total number of osteogenic sarcomas in this series. Of the osteoblastic variety two involved the skull, five the maxilla, six the mandible and one each the scapula and vertebrae. Of the total number of osteogenic sarcomas, only eight were below the ankle and wrist joints For detailed information regarding bones involved, the reader is referred to table 2 in the first chapter

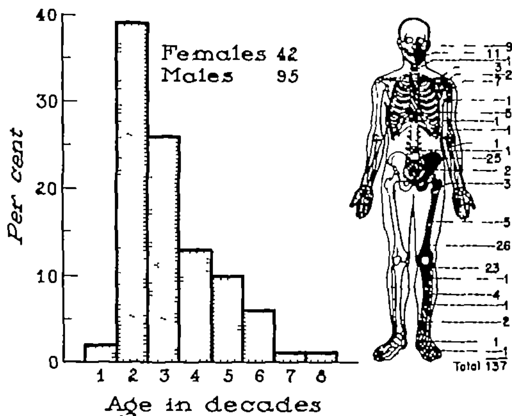


FIG. 17 2 Skeletal, age and sex distribution of chondroblastic osteogenic sarcoma.

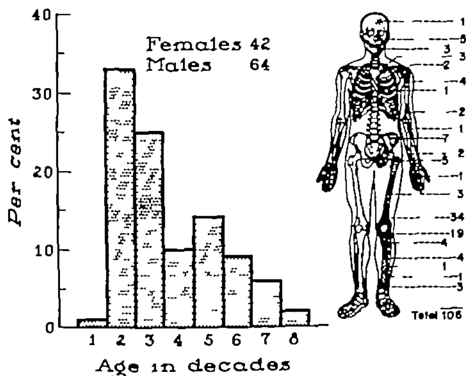


FIG 17 3 Skeletal, age and sex distribution of fibroblastic osteogenic sarcoma.

Skeletal, Age and Sex Distribution

Comparison of the data shown graphically in Figures 1 2 and 3 emphasizes the basic kinship of the three histologic types of osteogenic sarcoma. Males predominate in all types although this is somewhat more striking in the chondroblastic variety All three types have a predilection for the metaphyseal region of the long tubular bones. In this series chondroblastic osteogenic sarcoma had a slightly greater tendency to involve the trunk than did the other two types.

The age distributions were similar for all three types and contrary to some observations in the literature, no secondary peak was found in the older age groups This secondary peak of incidence has been blamed on the influx of sarcomas secondary to Paget s disease in older people. Perhaps this "secondary peak" is a spurious one that results from the natural tendency to report unusual cases.

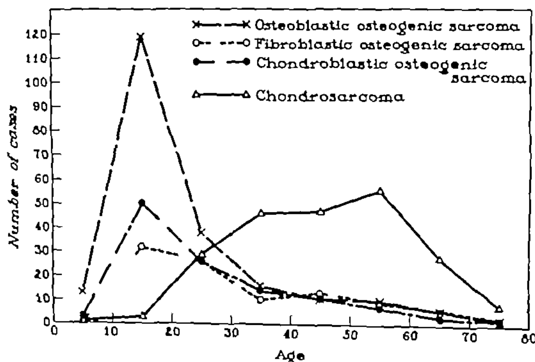


FIG 17-4. Age distribution of the various types of osteogenic sarcoma contrasted with that of chondrosarcoma. If the data for osteogenic sarcoma had been expressed in percentages rather than in numbers of cases, the lines representing the three types would have been practically superimposed. Note that there are practically no chondrosarcomas in the second decade, the age of peak incidence of all histologic types of osteogenic sarcoma. In middle and old age, when chondrosarcoma is common, the osteogenic sarcomas become increasingly rare

Symptoms

Pain and swelling are again the cardinal symptoms. They are, obviously nonspecific and for this reason one should not ignore the possibly serious nature of these complaints, especially when they occur in childhood, adolescence or young adulthood. Pathologic fracture is relatively uncommon.

The duration of symptoms prior to definitive therapy varies from a few weeks to several months. A history of trouble for more than 1 year is uncommon in patients with ordinary osteogenic sarcoma. Less than 2 per cent (eight cases) in the present series had pre-existing Paget's disease of bone as the basis of the osteogenic sarcoma. In some of these, the patients had had symptoms of osteitis deformans prior to the onset of the symptoms resulting from sarcoma.

Physical Findings

A painful mass in the affected region is usually apparent. Sometimes the mass is very large and then it may be associated with overlying engorged veins and even edema distal to the lesion. Physical examination is noncontributory in the case of some of the tumors that are covered by a thick layer of tissues. Evidence of pathologic fracture is distinctly uncommon.

Roentgenologic Features

Depending on the amount of ossification and calcification found in osteogenic sarcoma, there is great variation in the roentgenographic shadows produced. Tumors may be completely lytic or predominantly sclerotic, but they usually exhibit a combination of these features. The destructive process may be limited to the medulla but usually involves the cortex as well, since it is nearly always perforated by the growing tumor. There is a gradual transition from zones of marked lysis to zones of uninvolved bone, making the borders of the lesion indistinct. Nonneoplastic bone is deposited, sometimes in layers, when the periosteum is elevated by the perforating tumor. With continued development of the neoplasm one frequently sees a large soft-tissue mass contiguous to the bone.

Varying degrees of density are seen within the affected portion of bone when the osteogenic sarcoma produces calcifying and ossifying osteoid substance. These densities often extend into the contiguous soft tissues. The proliferated bone produced by the neoplastic cells characteristically has a streaked texture and ill-defined margins. The roentgenologic diagnosis is usually easily made in the case of those tumors that show a combination of destruction of bone and proliferation of new bone, but definitive therapy should never be recommended without confirmation by biopsy.

Osteoid substance, even if present in large amounts in an osteoblastic osteogenic sarcoma, produces no radiopacity if it is completely uncalcified.





FIG. 17-5. *a*, Osteogenic sarcoma of distal part of the femur with cortical destruction sufficient to produce pathologic fracture. *b*, Sclerosing osteogenic sarcoma of upper part of humerus, one of the more common sites for this tumor. Note the sunburst effect

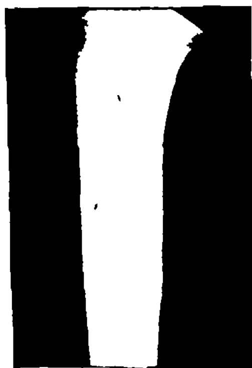


FIG. 17-6. Almost completely lytic, fibroblastic osteogenic sarcoma of upper central portion of tibia.



FIG. 17-7. Lytic and sclerotic sarcoma of upper part of metaphysis of tibia, the second commonest site of origin of osteogenic sarcoma



FIG. 17-8 (*above*) Chondroblastic osteogenic sarcoma of right ilium.



FIG. 17-9 (*right*) Lytic, but osteoblastic osteogenic sarcoma secondary to Paget's disease of the humerus.



FIG. 17-10 Osteogenic sarcoma of the distal portion of the femur. Note the destruction, sclerosis and "sunburst" effect.



FIG 17 11 Grade 4 osteoblastic sarcoma treated by hindquarter amputation. This operation has effected a survival of more than 10 years to the present time (Reproduced with permission from. Coventry M. B. and Dahlin, D C. *J Bone & Joint Surg* 39A 741 757 1957)





FIG 17 12 Early osteogenic sarcoma, inadvertently treated conservatively *b* Five and a half months later the tumor has produced obvious cortical perforation and other signs indicative of malignancy



FIG. 17 13 Recurrence along graft 3½ years after excision of upper end of humerus for a grade 1 osteosarcoma that was basically central and presumably made the patient an ideal candidate for conservative therapy Despite forequarter amputation, recurrence developed in the thoracic wall

Gross Pathology

By the time an osteogenic sarcoma receives definitive therapy it has breached the cortex, in the average case. The extraosseous mass may even completely encircle the bone The periosteum presents a barrier that often has become greatly distended before it is perforated. Slight to complete cortical destruction is found in the site of perforation.

Some of these tumors spread in the marrow cavity for surprising distances and this tendency must be reckoned with during ablative therapy In nearly all instances the extent of the marrow involvement is readily apparent grossly when one saws the bone longitudinally and most tumors do not spread beyond their gross extraosseous limits. Skip areas of medullary involvement are extremely rare.

Nearly all osteogenic sarcomas have such a prominent central component that a central origin is logically assumed Rarely however a highly malignant one is outside the bone and involves only the outer portion of the cortex, suggesting a periosteal origin.

As suggested by the roentgenogram, these tumors vary from extremely soft, friable and granular masses through a variety that is firm and fibrous with foci of irregular ossification and variable amounts of chondroid material, to the densely sclerotic ones. Sclerosis, when present, is invariably most pronounced in the

central regions. Nearly all osteogenic sarcomas, however sclerotic, have soft peripheral zones that can be sectioned without preliminary decalcification. Areas of necrosis, cyst formation, telangiectasis and hemorrhage are most likely to occur in the soft tumors.

Metastasis occurs almost exclusively by the hematogenous route, with the production of pulmonary deposits. Lymphatic dissemination is rare.

Extremely rare cases in which multiple primary osteogenic sarcomas occur have been described and the author has observed two examples of this type, but the possibility of the second lesion's being a solitary metastatic one could not be absolutely excluded in either of them.



FIG. 17 14 Type I osteoblastic osteogenic sarcoma of lower portion of femur. Hemorrhage and degeneration but practically no intramedullary spread are seen. The roentgenogram of this tumor is shown in Figure 17 5.

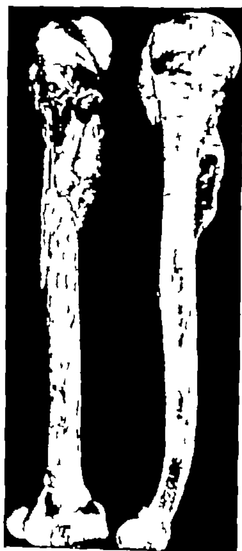


FIG. 17 15 Densely sclerotic osteosarcoma of upper part of humerus. Intramedullary spread nearly to the elbow has occurred.



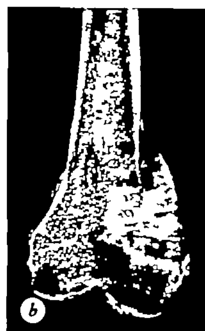


Fig. 17 16. Chondroblastic osteogenic sarcoma with areas of practically pure chondrosarcoma. This scapular tumor occurred in a 54-year-old woman. *b*, Fibroblastic osteosarcoma of distal part of femur Note cortical perforation, periosteal elevation, and typical metaphyseal location.

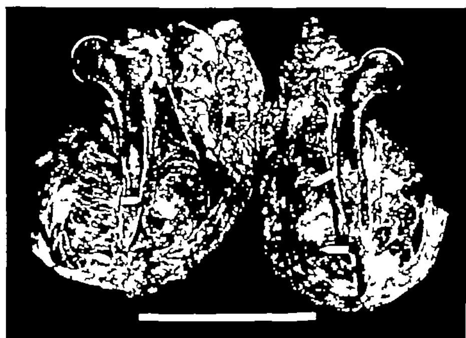


Fig 1 1 An unusual finding—recurrence in the stump after high amputation through the thigh for an osteogenic sarcoma of the low r end of the femur This may have been the result of implantation of tumor cells, if proper precautions were not observed since the biopsy immediately preceded the amputation. The primary tumor in this case was in the d stal 8 cm of the femur and there was no intramedullary spread.



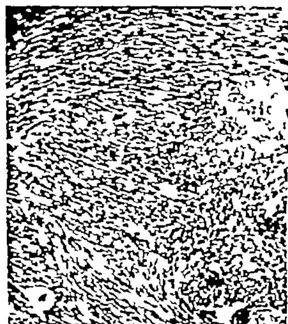


FIG 1 21 Osteoblastic osteogenic sarcomas *a* Typical lacelike pattern of uncalcified and (dark) calcified osteoid being produced by highly anaplastic cells (×200) *b* Densely sclerotic zone with shriveled cells compressed by osteoid (×100) *c* Large pools of blood in a hemorrhagic telangiectatic lesion (×35) *d* Extremely anaplastic osteogenic sarcoma with no osteoid production in this field (×165) (Figure 17 21*a* reproduced with permission from Coventry M B. and Dahlin, D C *J Bone & Joint Surg* 39A 741 757 1957)





FIG. 17.22. *a* (×110) and *b* (×115) are sections from two chondroblastic osteogenic sarcomas, both of which contain dominating chondroid substance, but both also contain distinct, lacy, darker-staining osteoid trabeculae that are derived *from neoplastic cells near the bottom of each picture. (Figure 17.22a* reproduced with permission from Coventry, *M. B.* and Dahlin, D. C.: *J. Bone & Joint Surg.,* *39A*:741-757, 1957.)



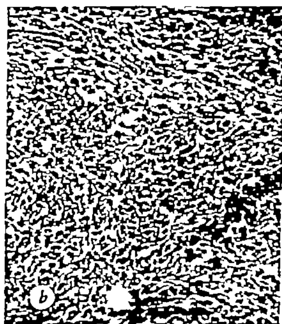


FIG. 17.23. *a* Fibroblastic osteogenic sarcoma, grade 2, showing a focus of chondrosarcoma in this field (×100). *b* Another area of this fibroblastic tumor which, however, is producing tumor osteoid in the lower portion of the picture (×185). (Figure 17.23 reproduced with permission from Coventry, M. B. and Dahlin, D. C.: *J. Bone & Joint Surg.,* *39A*:741-757, 1957.)

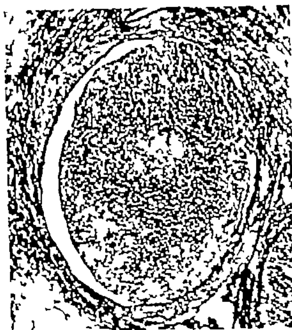


Fig. 17 4. Grade 3 chondroblastic osteogenic sarcoma of the upper end of the humerus, here shown in the lumen of a small regional vein (×70)



Fig. 17 25 Codman's reactive angle Striae of non-neoplastic bone are seen at right angles to the almost vertical broad trabeculae of the invaded cortical bone (×5)



Fig. 17 26 Grade 4 osteoblastic sarcoma In this zone the cells are so small they resemble those of Ewing's tumor and benign giant cells are present to confuse the issue further (×150)



Fig. 17 27 Osteogenic sarcoma producing irregular black masses of osteoid in a lymph node. This type of metastases is conspicuous because of its rarity (×65)

Treatment

Because osteogenic sarcoma is a radioresistant neoplasm, ablative surgical treatment is the procedure of choice. Surgical treatment of cancer aimed at cure is based on the premise that the tumor should be removed from the patient before metastasis becomes established. Metastasis obviously must occur at some specific time in the evolution of a given sarcoma. Accordingly some patients will pay with their lives when treatment is delayed unnecessarily. One must, of course, examine the patient and roentgenograms of his thorax for evidence of metastasis before instituting therapy.

Nearly all osteogenic sarcomas contain small or large foci that require no decalcification prior to sectioning and these foci routinely have the best cytologic details for diagnosis. Good fresh frozen sections are adequate for definitive diagnosis by one familiar with the pathology of bone.

Ordinarily in suspected osteogenic sarcoma of the extremities two tourniquets are applied, one above the tumor and one above the proposed site of amputation, thereby precluding the possible dissemination of tumor emboli by the biopsy procedure. Amputation is performed between the tourniquets after diagnosis by examination of fresh frozen sections of biopsy material. Extreme care should be employed to prevent implantation of tumor cells at the definitive amputation level. Those averse to diagnosis by fresh frozen sections should have permanent sections of nearly all osteogenic sarcomas ready for diagnosis in 1 day's time. Detailed study of heavily ossified portions of the tumor or adjacent cortical bone is rarely necessary in establishing the correct diagnosis.

A good rule is to amputate through the bone above the affected bone, but it requires modification in the treatment of the common sarcomas of the distal portion of the femur. Data have not yet proved whether disarticulation at the hip is preferable to amputation through the upper part of the femur for these. Since a small percentage of osteogenic sarcomas show marked spread in the marrow it is mandatory that the level of transection be checked to determine the adequacy of any amputation through the affected bone. Hindquarter amputations are necessary for tumors of the upper end of the femur and some of those in the innominate bone, and forequarter amputations for those of the upper part of the humerus. Lymph nodes are so rarely involved that dissection of nodes is probably not indicated unless they are enlarged.

Radical local excision should be employed whenever possible for those tumors not in the extremities. Local excision of osteogenic sarcoma in the extremities is rarely if ever indicated.

Radiation therapy is indicated for those tumors not amenable to ablative surgical treatment. Irradiation prior to amputation has been advocated recently but whether such treatment will affect the cure rate favorably or unfavorably is as yet unknown.

A [illegible] number of patients in whom a localized pulmonary metastatic growth develops after the primary one has been controlled have had pulmonary resection. The over all value of such resections for metastatic os[illegible] is not yet known, but some long-term cures have been effected.

Prognosis

Nineteen per cent of all the patients in this series treated more than 5 years previously survived 5 years, and 15 per cent of those eligible survived 10 years Ninety seven per cent of patients were traced Most of the 4 per cent who died in the period, 5 through 9 years after diagnosis succumbed to the effects of their tumors. For reasons unknown, tumors of the tibia were twice as curable as those of the femur the 5 year survival rates being 34 6 and 17 0 per cent respectively The histologic type affected prognosis, the 5-year survival rate for the osteoblastic, chondroblastic and fibroblastic types being 15.6 22.7 and 22.9 per cent respectively The highly undifferentiated sarcomas (Broders grades 3 and 4) had but a slightly poorer prognosis than did those of combined grades 1 and 2 and surprisingly only one of the six patients with grade 1 lesions was cured. Contrary to common belief survival rates for young patients were somewhat better than those for older patients None of the eight patients who had sarcoma as a complication of Paget s disease was cured, and the literature indicates only one cure in more than 100 patients who had such tumors.

These relatively favorable data on a large series of patients should help dispel the unfounded notion held by some that the prognosis of osteogenic sarcoma is so poor that prompt and proper therapy is useless.

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Chapter 18

Parosteal Osteogenic Sarcoma (Juxtacortical Osteogenic Sarcoma)

THIS TUMOR is considered separately from the remainder of the osteogenic sarcomas because it is distinctly less malignant and, therefore, has a vastly different clinical behavior. As the name implies, this tumor is on the outer surface of the cortex of a bone, and some prefer to call it a juxtacortical sarcoma.

The rarity of this lesion, comprising less than 5 per cent of osteogenic sarcomas, has delayed its general recognition. Although occasional typical cases were documented in the literature, it was not until the description of a collected series by Geschickter and Copeland in 1951 that the entity was established. There are gradations from the even more uncommon, completely benign parosteal osteoma, through the lesion with minimal evidence of malignancy to the frankly malignant, though fairly well-differentiated, parosteal tumor. It is obvious that when the diagnosis of sarcoma depends on such subtle changes as are found in some of these tumors the problem is often a difficult one.

Osteogenic tumors of a high degree of malignancy histologically (that is, of high grade by the method of Broders) are occasionally seen predominantly on the surface of a bone but they do not belong in the category under discussion. Inclusion of tumors that are histologically like the ordinary osteogenic sarcoma or fibrosarcoma will decrease the usefulness of the term "parosteal osteogenic sarcoma."

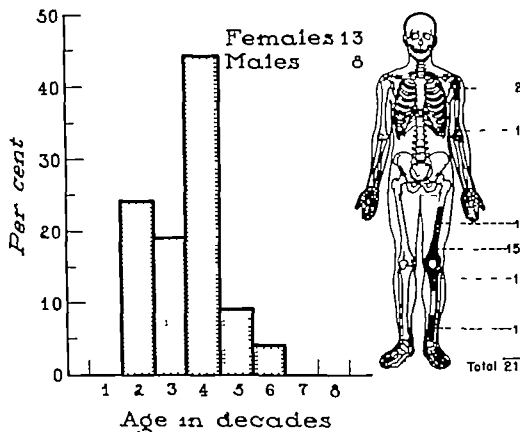


FIG. 16-1 Skeletal, age and sex distribution of parosteal osteogenic sarcoma.

Incidence

Parosteal sarcoma is a distinctly rare neoplasm. It comprised only slightly more than 1 per cent of the Mayo Clinic series of malignant tumors primary in bone

Sex

Females constituted 62 per cent of the patients in this series, but the ratio was practically the reverse in the series of patients reviewed by Geschickter and Copeland.

Age

The average age of patients with this tumor is greater than that of those with ordinary osteogenic sarcoma, a difference that can be explained at least in part by its slow growth.

Localization

Practically all of the recorded parosteal osteogenic sarcomas have involved the femur humerus and tibia, in that order of frequency Other bones may however be affected. By far the most common site for its development is the distal portion of the shaft of the femur posteriorly In common with the ordinary osteogenic sarcoma, this lesion most often affects the metaphyseal region.

Symptoms

Swelling is the most important symptom. Because of the inherent slow growth of the tumor the swelling is often of several years duration. Sometimes the patient has noted swelling for only a few days or weeks, when it is obvious from the roentgenograms and the pathologic characteristics that the lesion had been present for much longer The tumor may be painful.

A common and practically pathognomonic history is as follows Several years previously the patient underwent excision of a tumor that had been considered to be an atypical osteochondroma roentgenologically The pathologist regarded it as an unusual osteochondroma, and perhaps described it as cellular In the interim, the tumor may or may not have required repeated excision because of recurrence. When seen now there is a recurrent ossified juxtacortical mass in one of the sites of predilection.

Physical Findings

A mass at the lesional site which is sometimes painful to pressure, is the only significant physical finding. The mass may be of enormous size

Roentgenologic Features

The tumor is seen to be juxtacortical and usually has a remarkable tendency to encircle the shaft. This is best demonstrated by stereoscopic roentgenograms. It is seen to be firmly attached to the cortex along a part of its broad base but it tends to grow peripherally in mushroom fashion to lie in close proximity to, but not necessarily attached to, the remainder of the underlying shaft which it encircles. In most cases, therefore, there is a partial free space of varying length and 1 to 3 mm. in thickness between the tumor and the underlying bone Ordinarily the tumor is lobular in outline, but sometimes angular projections extend into the soft tissues. From 75 to 90 per cent of the tumor s bulk shows a variable, usually marked, degree of ossification The periphery of the tumor is typically less ossified than its base. Numerous poorly defined and irregular radiolucent defects are ordinarily seen in the substance of the tumor because of zones of irregular fibrous or cartilaginous tissue Ordinarily the osseous mass is amorphous, but occasionally true osseous trabeculation may be observed Periosteal elevation at the edge of the tumor and consequently Codman s angle are conspicuously absent. Medullary involvement ordinarily does not occur except in extremely long-standing tumors or especially in tumors that have been previously treated unsuccessfully E en recurrent tumors, however are usually still juxtacortical.

The roentgenogram is important in the differential diagnosis The heterotopic bone seen in myositis ossificans usually shows a well-organized and clear-cut trabecular pattern in contrast to what is seen in parosteal osteogenic sarcoma. Although the lesion of myositis ossificans may abut on a bone and especially overlap it when seen on only one roentgenographic projection, careful study will show that it does not have the characteristic broad base of parosteal osteogenic sarcoma. Osteochondroma (osteocartilaginous exostosis) can ordinarily be differentiated with assurance from parosteal osteogenic sarcoma

from the roentgenographic standpoint. The continuity of the bony cortex with the pedunculated or sessile base of an osteochondroma as well as the continuity of the cancellous bone with the core of an osteochondroma is absent in parosteal osteogenic sarcoma. Evidence of cortical destruction, extensive medullary involvement, Codman's reactive angle and an ill-defined border differentiate ordinary osteogenic sarcoma from parosteal osteogenic sarcoma. Occasional benign parosteal osteomas which in the author's experience are much less common than the malignant counterpart under discussion, may be impossible to differentiate on a roentgenographic basis. This fact is not surprising when one realizes the differentiation is so subtle than it can sometimes be made with no real assurance even by the histopathologist.

Gross Pathology

Although these tumors merge with the cortex of the affected bone, they do not disrupt it until late, and ordinarily only after one or more recurrences following inadequate therapy. Accordingly medullary involvement is a late phenomenon if it occurs at all.

As indicated by the roentgenograms, these tumors are predominantly ossified. Ordinarily however

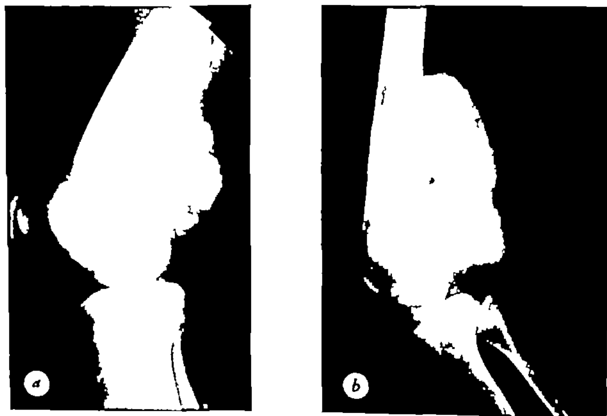
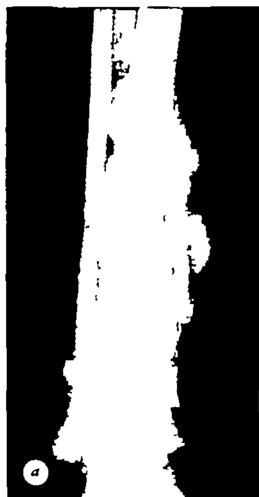


FIG 18-2 Parosteal osteogenic sarcoma of lower portion of shaft of femur posteriorly. Without stereoscopic views, the absence of medullary involvement is not apparent. The tumor recurred within a year after local excision. *b* This tumor of the femur had been present for 7 years. At the time of biopsy and amputation, zones of grade 2 sarcoma were present, but there was still no medullary involvement. (Reproduced with permission from Dwinnell, L. A., Dahlin, D. C. and Ghormley, R. K.: *J Bone & Joint Surg* 36A:732-744, 1954.)



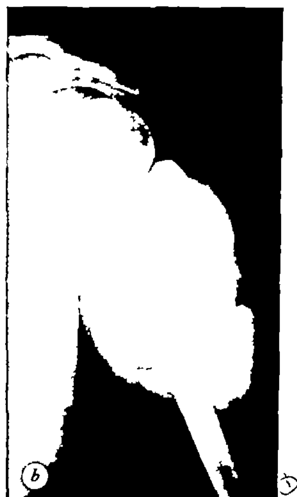


FIG 10-3. *a*. Parosteal osteogenic sarcoma of tibia. Excision was followed by recurrence and eventual death from metastasis. *b*. This parosteal sarcoma encased the upper portion of the shaft of the humerus. Local removal was unsuccessful in controlling the lesion. (Reproduced with permission from Dwinnell, L. A., Dahlin, D. C., and Ghormley R. K. *J Bone & Joint Surg* 36A:732-744, 1954.)

there are softer fibrous foci, especially near or at the periphery of the neoplasms. These zones are the ones most likely to afford histologic evidence of malignancy. Small or prominent chondroid foci are often found in these lesions.

Recurrent tumors of this type, especially when they show an increased degree of malignancy histologically, may be only slightly sclerotic if at all. In fact, such lesions may simulate closely the appearance of ordinary osteogenic sarcomas.

Myositis ossificans, which must be considered in the differential diagnosis, is often completely separated from the bone. When it does abut on bone it rarely coapts itself to the cortex so as to produce an extensive broad base such as that seen in parosteal osteogenic sarcoma.



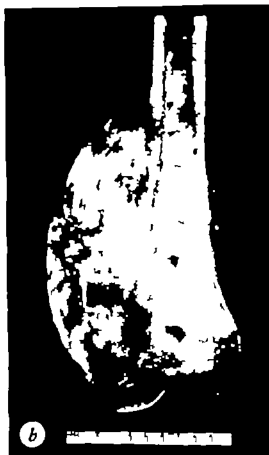


FIG. 18-4. *a*. Cut surface of parosteal osteogenic sarcoma illustrated in Figure 18-2*a*. Local excision was followed by recurrence within a year, and amputation was performed. *b* Gross specimen of the lesion shown in Figure 18-2*b* Although this tumor had been present for 7 years, there was no medullary involvement. (Reproduced with permission from Dwinnell, L. A Dahlin, D C. and Ghormley R. K. *J Bone & Joint Surg* 36A 732 744, 1954)



FIG. 18-5 Although this tumor resembles parosteal osteogenic sarcoma of the ordinary type it is actually a high-grade osteogenic sarcoma and does not belong in the indolent pathologic variety under discussion.

Histopathology

The most prominent feature of parosteal osteogenic sarcoma is its component of rather regularly arranged osseous trabeculae. Apparently the more immature trabeculae undergo maturation in this slowly developing tumor and become normalized Between these more or less normal trabeculae are atypical, proliferating, spindle-shaped or polyhedral cells in which one finds occasional or sometimes fairly numerous mitotic figures. The spaces between the trabeculae are not filled with fat or hematopoietic cells as in osteochondroma. This fact alone serves clearly to differentiate osteocartilaginous exostosis from parosteal osteogenic sarcoma. The same atypical spindle cell elements alluded to make up the purely fibrous zones of these tumors. Evidence of malignancy may be found only in small foci, making it necessary to study multiple sections for accurate appraisal Variable amounts of osteoid are found deposited in the proliferating spindle cell stroma, apparently owing to metaplasia of the basically fibroblastic cells into a type capable of producing osteoid. Islands of chondrosarcoma are commonly seen in these tumors.

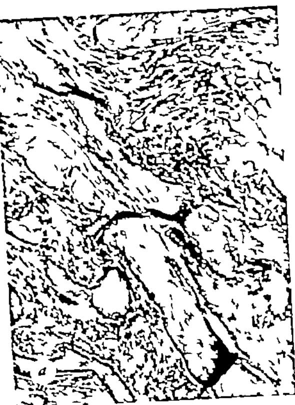
Occasional tumors in this group show an increase in histologic activity with recurrence.

The majority of parosteal osteogenic sar... reveal, at their peripheries, an intermixing with muscle and fat cells. This finding has added to th... confusion that exists in the differentiation of this malignant tumor from myositis ossificans, and patholo...ically suggests a kinship with desmoid tumors of the soft tissues of the extremities.

Differentiation of this malignant tumor from myositis ossificans histologically depends on the lack of true anaplasia in the proliferating cells of the latter lesion. Gross and roentgenographic guidance should direct one's suspicion, as indicated above A history of sudden onset, sometimes after significant trauma, is strong evidence in favor of myositis ossificans



FIG. 18-6 Typical microscopic field from a parosteal osteogenic sarcoma. Note well formed osseous trabeculae separated by actively proliferating fibroblastic tissue that is undergoing metaplasia to a type capable of producing osteoid substance and bone (×100)



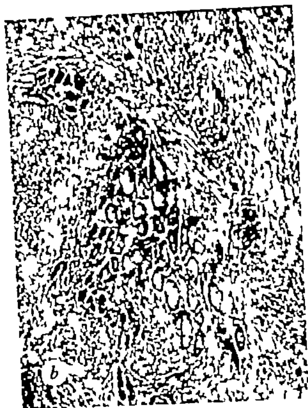


FIG. 18- *a.* Relatively well-formed osseous trabeculae with intervening fibroblastic tissue and chondroid zone (×100). *b.* Periphery of parosteal osteogenic sarcoma showing invasion of striated muscle, large fibers of which are here shown in cross section (×80). (Reproduced with permission from Dwinnell, L. A., Dahlin, D. C. and Ghormley, R. K.: *J. Bone & Joint Surg.* 36A 732-744, 1954.)

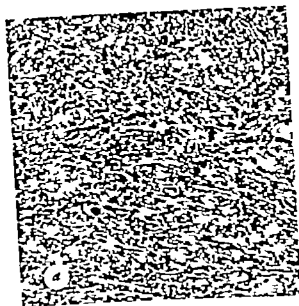




FIG. 18-8. *a.* Peripheral zone of grade 2 fibrosarcoma in tumor illustrated in Figures 18-2*b* and 18-4*b*. *b.* Island of chondrosarcoma from one of these tumors (×[illegible]00). (Reproduced with permission from Dwinnell, L. A., Dahlin, D. C. and Ghormley, R. K.: *J. Bone & Joint Surg.* 36A:732-744, 1954.)



Fig. 18-9 Nodule of metastatic parosteal osteogenic sarcoma in lung (×100) Death from metastasis occurred 20 years after the first surgical treatment for a lesion of the distal portion of the femur and 6 years after amputation.





Fig. 18-10 *a*, High grade osteoblastic (×200) and, *b*, high-grade fibroblastic (×80) osteogenic sarcomas. Both of these were found in recurrent tumors that followed local excision for parosteal osteogenic sarcoma. (Figure 18-10*b* reproduced with permission from Dwinnell, L. A., Dahlin, D. C. and Ghormley, R. K. *J. Bone & Joint Surg.* 36A:732-744, 1954.)

Treatment

A dogmatic stand regarding therapy of this lesion cannot be based on any sizable series of cases in which optimal treatment has been given early because no such series exists. Too often the primary treatment has been inadequate as judged by the high rate of recurrence.

The experience at the Mayo Clinic and an analysis of many of the relevant cases recorded in the literature force the following conclusions. If the tumor has indisputable, albeit minimal, histologic evidence of malignancy amputation is the treatment of choice for those tumors that are large or recurrent. For small, nonrecurrent parosteal osteogenic sarcomas it is perhaps feasible to employ local excision or segmental resection, but the surgeon must be able to encompass the tumor widely getting well into normal bone

If critical analysis, which may require study of the entire tumor, fails to uncover proof that the tumor is malignant, wide local excision and careful follow-up studies are indicated.

A factor of importance in contemplating conservative management is that a minority of these tumors increase in histologic activity with recurrence and some become highly malignant, rapidly metastasizing sarcomas

Prognosis

Five-year survival data are meaningless because of the slow growth of parosteal osteogenic sarcomas. Four of the series of 15 patients reported by Dwinnell and associates are now known to have died with pulmonary metastasis All of these had at least one recurrence before amputation was performed.

The indolent behavior of parosteal osteogenic sarcoma is emphasized by one of the fatal cases. A recurring tumor of the lower end of the femur was subjected to six excisions during a 14-year period. Then amputation was performed but the patient succumbed, with proved pulmonary metastases, 6 years after amputation and 20 years after the first excision.

Earlier ablative surgical treatment should effect a high rate of cure

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Chapter 19

√ Ewing's Tumor

EWING'S TUMOR is a distinctive, small round cell sarcoma that is the most lethal of the bone tumors. It is the subject of controversy in the literature because of the somewhat nonspecific histologic characteristics of the tumor which is composed of solidly packed, small round cells. Until recently some of the small cell osteogenic sarcomas, most of the reticulum cell sarcomas, and even benign conditions such as eosinophilic granuloma were at times classified with Ewing's tumor.

It is sometimes impossible to differentiate a biopsy specimen of a metastatic malignant tumor such as neuroblastoma or small cell cancer of the lung from a specimen of Ewing's tumor even after critical histologic study according to modern concepts. From the practical standpoint, however, when the physician is confronted with what is clinically a primary lesion in bone that is typical of Ewing's tumor, he is obliged to treat it as such. Armchair meditations regarding whether the tumor being appraised may possibly be a metastatic lesion from an undisclosed primary tumor can usually be verified only after studies at necropsy.

Speculation regarding the possible origin of the cells that comprise Ewing's tumor is fruitless, and it seems best to regard them as arising from undifferentiated mesenchyme.

Although Ewing's tumor and reticulum cell sarcoma can be distinguished histologically in the majority of cases, occasional tumors appear to fall midway between them. In the present series there were 27 such tumors. They contained cells that were larger and somewhat more irregular than those of classic Ewing's tumor. All but one of these caused death of the patient and, accordingly, they were included with Ewing's tumors rather than segregated as a new tumor type.

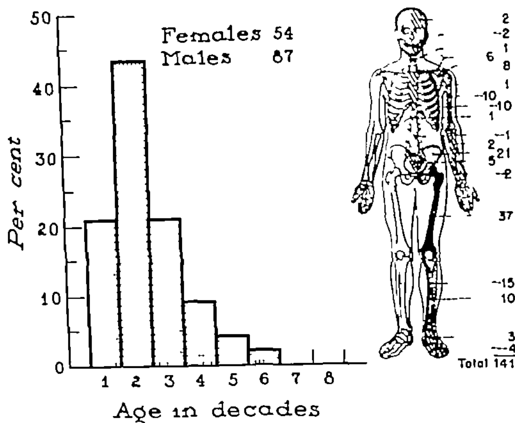


FIG. 19-1 Skeletal, age and sex distribution of the combined group of typical Ewing's tumor and the rare, large cell type.

Incidence

Ewing's tumor comprised somewhat less than 10 per cent of the total malignant tumors in the Mayo Clinic series.

Sex

Ewing's tumor is slightly more common in males.

Age

The persons affected by this tumor are, on the average, younger than those affected by any other primary malignant tumor of bone. The youngest patient in the present series was 18 months of age. The 27 tumors composed of somewhat larger cells than usual occurred at a slightly older average age. When confronted with the problem of Ewing's tumor in patients who are past the third decade of life, one must be especially careful to exclude metastatic carcinoma.

Localization

A majority of Ewing's tumors are in the extremities but any bone of the body may be involved. Any portion of a long tubular bone may be affected Eight of the tumors in this series involved the spinal column, including the sacrum. The skull, the mandible, the radius and the ulna each accounted for two tumors, the sternum for one the clavicle for six, the scapula for eight and the ribs for 10

Symptoms

Pain and swelling are the commonest symptoms of Ewing's tumor. Pain is the first symptom in well over half the cases, and it tends to increase in severity with time. Although swelling in the region of the tumor is very common by the time the patient seeks medical advice, it is rarely the first symptom. Pathologic fracture is relatively rare. The average patient has had symptoms for approximately 9 months before he seeks medical care.

Physical and Laboratory Findings

The majority of patients have a palpable tender mass and some have dilated veins over the tumor.

Patients with Ewing's tumor frequently have an elevated temperature, often associated with some secondary anemia, and sometimes with leukocytosis. These findings may suggest that the osseous lesion is inflammatory in origin. It has been found that Ewing's tumor, when associated with these systemic features, has a prognosis that is even worse than average.

Roentgenologic Features

Ewing's tumor tends to be extensive, sometimes involving the entire shaft of a long bone. Even so, more of the bone will be found involved pathologically than was obvious from the roentgenogram, in the average case. A combination of lytic destruction and regions of density owing to stimulation of new bone formation is characteristic. As the tumor bursts through the cortex, which may show only minimal roentgenographic changes, it often elevates the periosteum in stages. This produces the characteristic multiple layers of subperiosteal reactive new bone which gives the "onion-skin" appearance of Ewing's tumor. Radiating spicules from the cortex of an affected bone are not uncommon, a fact which complicates the differentiation from osteogenic sarcoma. When the initial roentgenogram shows extensive destruction of bone combined with a large extraosseous mass the lesion is usually clearly malignant. Occasionally Ewing's tumor produces an expansion of the affected bone.

Experienced observers have concluded that although Ewing's tumor can sometimes be diagnosed with a high degree of assurance from its roentgenologic features and although it very often produces features that are virtually pathognomonic of malignant bone tumor, there are a number of conditions that can produce a similar picture. Among these are acute or chronic osteomyelitis, eosinophilic granuloma, reticulum cell sarcoma, metastatic malignant tumor and even osteogenic sarcoma.

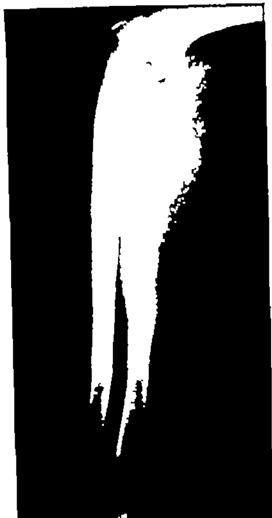


FIG. 19-2 (*above*). Ewing's tumor of radius. Note the prominent radial spicules in the periosseous tissues. (Reproduced with permission from McCormack, L. J., Dockerty, M. B., and Ghormley, R. K.: *Cancer* 5:85-99, 1952.)



FIG. 19-3 (*above right*). Ewing's tumor of humerus showing multiple layers of subperiosteal, reactive, new nonneoplastic bone. (Reproduced with permission from McCormack, L. J., Dockerty, M. B., and Ghormley, R. K.: *Cancer* 5:85-99, 1952.)



FIG. 19-4 (*right*). Ewing's tumor in region of acetabulum and adjacent ischium. Note the periosseous irregular densities.



FIG 19-5 Ewing's tumor of fibula The gross lesion is shown in Figure 19



FIG 19-6 Ewing's tumor of tarsal bones An attempt had been made to produce arthrodesis, pursuant to an erroneous diagnosis

Gross Pathology

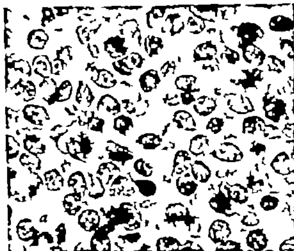
Solid masses of viable tumor are characteristically gray white, moist, glistening and somewhat translucent. They may be almost liquid in consistency Tumor frequently invades bone beyond the limits suggested by the roentgenogram Zones of necrosis hemorrhage and even cyst formation are common The neoplastic tissue is often admixed with proliferating bony and fibrous tissue in the periosseous regions.

The medullary cavity appears to be the site of origin of these tumors. Although they may affect any portion of a long bone and commonly involve a great length of it, the bulk of the tumor is frequently in the metaphyseal region.

Metastasis is characteristically to the lungs and to other bones. The latter feature is so prominent that some have suggested that Ewing's tumor may have a multicentric origin.



FIG 19-7 Gross specimen from the case represented in Figure 19-5



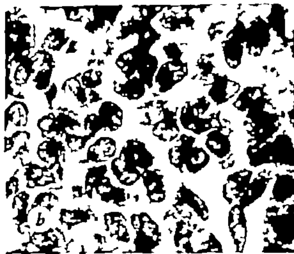


FIG 19-1.— *a* Typical Ewing's tumor with round and oval nuclei, all of approximately the same size (×800) *b* The larger-cell type of Ewing's tumor Note that the nuclei are more irregular in shape (×800)

Treatment

Opinion is divided as to whether irradiation or ablative surgical treatment is best for Ewing's tumor. The low incidence of cure makes it impossible to procure convincing data on this point. Amputation has the advantage that it assures control of the local lesion. It sometimes becomes necessary as a palliative measure whether the primary tumor has been irradiated or not. Inoperable or metastatic masses should be irradiated.

Prognosis

Without question, Ewing's tumor is the most lethal of the primary malignant tumors of bone. Apparently reliable reports in the literature give 5 year survival rates that vary from zero to 12 per cent.

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Chapter 20

Malignant Giant Cell Tumor

TO BE CERTAIN of the diagnosis of malignant giant cell tumor the pathologist must be able to demonstrate zones of typical benign giant cell tumor in the malignant neoplasm under appraisal or in previous tissue obtained from the same neoplasm When confronted with an obviously malignant growth that contains a few or many benign osteoclastlike giant cells one can prove a relationship to benign giant cell tumor in no other way This is true because other neoplasms of bone including many of the osteogenic sarcomas contain a scattering or many of these benign giant cells

With this absolute type of definition of malignant giant cell tumor nine of the 11 such tumors in the present series followed treatment for typical benign giant cell tumors—tumors that contain no feature that distinguishes them from the remainder of the group of giant cell tumors. Eight of these nine secondary malignant tumors followed benign giant cell tumors at intervals that averaged more than 7 years from the time of treatment of the benign neoplasm, treatment that included radiation therapy in each instance. In these eight instances, the malignant tumor completely overran and destroyed any evidence of the original benign tumor The ninth secondary malignant tumor developed 1½ years after simple curettage of the benign giant cell tumor and remnants of it remained at the time of amputation. The tenth and eleventh tumors in this group contained an admixture of benign and malignant elements at the time of the first and definitive radical operation

Increasing evidence is being accumulated that irradiation may be influential in triggering the malignant transformation of a variety of osseous lesions, especially giant cell tumor

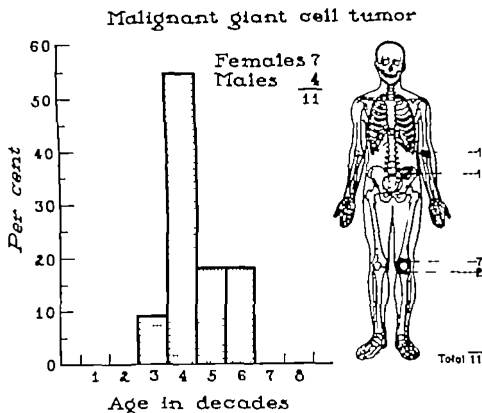


FIG. 20-1 Skeletal, age and sex distribution of malignant giant cell tumor

Incidence

The malignant giant cell tumors comprised less than 1 per cent of the total group of malignant tumors and 10 per cent of the giant cell tumors.

Sex

In this small group females predominated by nearly 2 to 1 whereas they constituted 55 per cent of the cases of benign giant cell tumor

Age

These patients were somewhat older on the average, than were those with benign giant cell tumor This is at least partially explained by the fact that most of the tumors developed several years after treatment of their benign precursors.

Localization

The distribution of these tumors is not significantly different from that of those benign giant cell tumors that do not undergo malignant transformation. As may be seen above, nine of them involved the region of the knee one was in the lower end of the humerus and one in the ilium.

Symptoms

These 11 patients had the symptoms of ordinary benign giant cell tumor at the outset. In four of the nine whose original tumor was completely benign, clinical or roentgenologic evidence developed that was considered to represent recurrence of benign giant cell tumor and necessitated retreatment during the interval between the first therapy and the development of proved sarcoma. As mentioned, eight of the 11 malignant tumors occurred an average of 7 years after the histologic diagnosis of benign giant cell tumor and therapy included irradiation in each of these. The ninth patient whose original lesion was completely benign as far as could be determined presented with a mixed benign giant cell tumor and high-grade sarcoma 1½ years later. The two patients whose original giant cell tumors contained malignant foci did not have remarkable histories.

It should be stressed that when the originally benign giant cell tumors became sarcomas, the clinical features changed abruptly from those of slowly progressing giant cell tumors to those of the rapidly growing sarcomas.

Physical Findings

The physical examination reveals only the evidence likely to be presented by any malignant tumor. Of course the tumor is almost certain to be at the end of the bone when it affects a long bone.

Roentgenologic Features

Roentgenologic changes do not differ from those described for fibrosarcoma or osteogenic sarcoma of bone. The classic features of malignant destruction are present and usually the process is completely lytic. Earlier roentgenograms of the lesion ordinarily afford evidence of the pre-existing benign giant cell tumor. Sometimes the malignant change is reflected in the roentgenogram considerably later than its occurrence had been suggested by the clinical history.



FIG. 20-2 Grade 4 fibrosarcoma of lower end of humerus. This tumor arose at the site of a benign giant cell tumor that had been treated by excision and irradiation 8 years previously. Despite amputation, death occurred within 1 year.

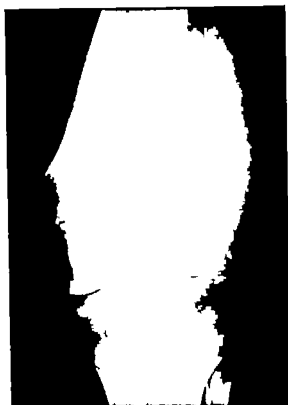




FIG. 20-3. *a* (*above*) and *b* (*above right*) Antero-posterior and lateral views of benign giant cell tumor of the lower end of the femur It was treated by insertion of radium following curettage. *c* (*right*) The same lesion 2 years after treatment. Two years after this roentgenogram was taken the leg was amputated for grade 3 fibrosarcoma which had completely replaced the original benign tumor

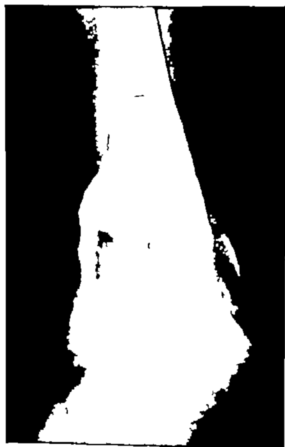




FIG 20-4 Anteroposterior and lateral views of benign giant cell tumor of upper end of left tibia. It was curetted in 1943 and given roentgen therapy in 1944 *b* The same lesion in 1948. By this time a grade 3 fibrosarcoma had replaced the benign tumor and despite amputation, the patient died with pulmonary metastasis 3 years later (Figure 20-4a reproduced with permission from Sabanas, A. O Dahlin, D C Childs, D S Jr and Ivins, J C *Cancer* 9 528-542, 1956)

Gross Pathology

The rare, malignant giant cell tumor that shows both benign and sarcomatous zones at the time of the first treatment is grossly indistinguishable from its benign counterpart. It produces variable degrees of expansion of the end of a bone, and it is ordinarily contained by the expanded periosteum. The commoner secondarily malignant giant cell tumor exhibits characteristic evidence of sarcoma such as invasion of surrounding osseous and soft tissues, hemorrhage and necrosis, although the last two of these are by no means uncommon in genuine benign giant cell tumor. The gross appearance of these secondary sarcomas will often have been modified by previous treatment which commonly includes the incorporation of bone grafts into the defect that follows curettage. Such grafts will have been partially or completely dissolved.

In general, the gross features of malignant giant cell tumor are not specific, and frequently it requires multiple microscopic sections to establish that foci of sarcoma are present in a lesion that still contains benign regions.



FIG. 20-5 Malignant giant cell tumor of lower end of femur. Roentgenograms of this lesion are shown in Figure 20-3

Histopathology

In most cases in my experience when sarcomatous change has occurred, the pre-existing benign giant cell tumor is no longer recognizable as such. The sarcoma that replaces it is ordinarily overtly malignant and presents no problem in diagnosis. In fact, in eight of these in this series that were originally completely benign, one could not have suspected a relationship to benign giant cell tumor from study of the subsequent sarcoma. Seven of these secondary tumors were pure fibrosarcomas and one was an osteogenic sarcoma. In the three other tumors, one of which had had previous surgical therapy there were foci of sarcoma admixed with the pattern recognizable as benign giant cell tumor. The sarcomas apparently arise from the stromal cells.

Careful review of the numerous tissue sections of the benign tumors in this series that subsequently underwent malignant change offered no histologic clue by which one might differentiate them from those that remained benign. Furthermore, the giant cell tumors that recurred after conventional therapy were not distinguishable from those that did not. Grading of bona fide giant cell tumors on a histologic basis does not appear to have any practical value, contrary to some assertions in the literature.





FIG. 20-6. *a* Benign giant cell tumor of distal end of femur (×175). *b* Recurrent tumor, 1½ years later, contained foci of sarcoma like that shown above, admixed with typically benign areas of giant cell tumor (×175).





FIG. 20-7. *a*, grade 4 fibrosarcoma (× 60) and *b* osteogenic sarcoma (×160). Both of these malignant tumors occurred at the sites of benign giant cell tumors that had been treated several years previously by a combination of surgery and irradiation. (Reproduced with permission from Williams, R. R., Dahlin, D. C., and Ghormley, R. K.: *Cancer* 7:764–773, 1954.)

Treatment

When indisputable evidence of malignant change is found in a giant cell tumor or in the zone previously occupied by one, ablative surgical treatment is the procedure of choice The sarcoma that develops is characteristically radioresistant being either fibrosarcoma or osteogenic sarcoma. The same principles outlined for the treatment of these sarcomas when they occur primarily should be followed Irradiation, at least as a palliative measure, may be employed for tumors not amenable to ablation.

Prognosis

When frankly malignant transformation has occurred in a benign giant cell tumor its prognosis is that of the sarcoma present. Six of eight patients with secondary malignancy have succumbed, and the ninth patient was operated on too recently for final evaluation. The two patients with tumors composed of mixed benign and malignant components at the time of the first operation were cured, one by amputation and one by en bloc excision of the affected segment of bone.

In none of the Mayo Clinic series did a benign giant cell tumor give rise to proved or even suspected metastasis. Only a few such metastasizing tumors have been reported.

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Chapter 21

Adamantinoma

ADAMANTINOMA of long bones is a peculiar epithelial neoplasm which appears to arise within the osseous substance. The origin of the epithelium that gives rise to this tumor is unknown. Some have postulated traumatic implantation, a concept that is favored by the fact that almost all reported adamantinomas have occurred in bones near the cutaneous surface. Others have expressed the belief that congenital rests of epithelium may be the source of these tumors. Still others have stated the view that the so-called adamantinoma of long bones is not epithelial at all but represents rather an unusual manifestation of some sarcoma, especially synovial sarcoma.

Despite this controversial literature the fact remains that there is a small group of epithelial tumors that present as primary lesions of bone. The name adamantinoma was given to these tumors because of their histologic resemblance to the common adamantinoma (ameloblastoma) of the jawbones. These odontogenic tumors of the jaws and the histologically related tumor that arises from Rathke's pouch are excluded from the discussion that follows.

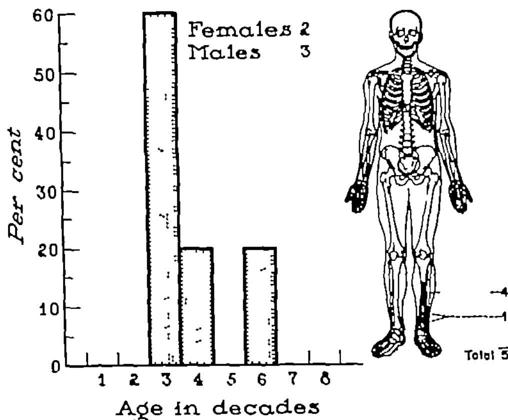


Fig. 21 1 Skeletal, age and sex distribution of adamantinoma.

Incidence

Approximately 30 examples of adamantinoma of long bones have been recorded in the literature The five cases in the Mayo Clinic series comprised less than one third of 1 per cent of the malignant primary tumors of bone.

Sex

No distinct sex predilection has become apparent in the few recorded cases

Age

The ages of patients with this tumor have varied from 12 years through the sixth decade of life

Localization

Practically all reported adamantinomas of long bones have involved the tibia, but examples have been described in the radius, ulna, femur and fibula. Most of these tumors have been in the middle portion of the affected bone

Symptoms

The prolonged clinical course of many patients with this tumor indicates its slow rate of growth in the average case. Pain is the most common initial symptom, whereas local tumefaction is the first complaint in a minority of cases. The duration of symptoms prior to diagnosis has varied from a few months up to 17 years.

Physical Examination

A mass which may be painful is the only physical finding of consequence.

Roentgenologic Features

In most cases the tumor appears as a well-defined, sometimes trabeculated area of rarefaction in the shaft of the tibia near its midportion. Long-standing tumors may attain great size and produce considerable expansion of the contour of the bone. Cortical break-through is distinctly unusual in patients that have not been treated, and reactive periosteal formation of new bone is rarely observed.

Rarefied areas that resemble those of fibrous dysplasia histologically have been seen in the tibia distal to the neoplasm, and a similar change was noted in the adjacent fibula in one of the cases in this series.

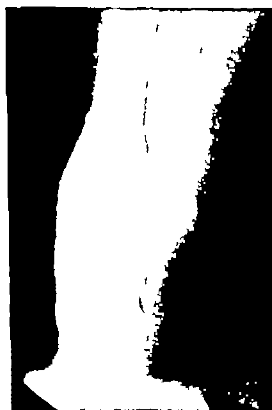


FIG. 21.2. Adamantinoma of tibia of 27-year-old woman. She had noted swelling for 8 years. The lesion was removed by curettage, but despite initial improvement amputation became necessary 16 years later. The nature of the lesion at the time of amputation is not known.

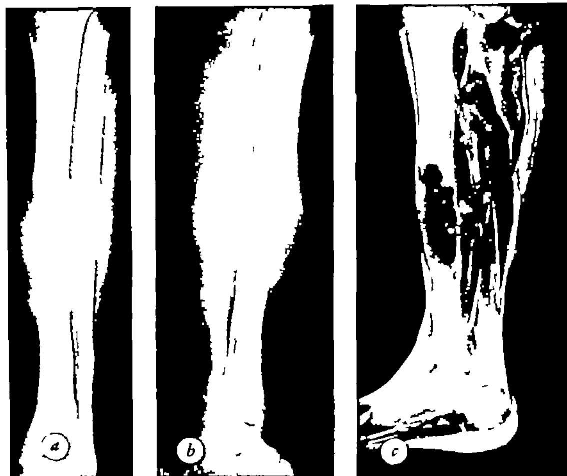


Fig 21 3 *a* and *b* Anteroposterior and lateral views of adamantinoma of tibia of 24-year-old man. A surgical procedure had been performed elsewhere 15 months previously The defects seen in the fibula and in the lower portion of the tibia were composed of fibrous tissue. *c* Amputated specimen showing the defect produced by curettage that had been performed 9 days previously (Reproduced with permission from Dockerty M. B. and Meyerding, H. W., *J.A.M.A.*, 119 932 937 1942)

Gross Pathology

Ordinarily adamantinomas are clearly delimited peripherally as indicated by the roentgenograms The surface is often somewhat lobulated. In most of the recorded cases the tumor has been gray or white and has varied in consistency from firm and fibrous to soft and brainlike. Occasionally cystic cavities are encountered Some of the tumors burst through the overlying cortex, but this is unusual in patients that have not been subjected to surgical therapy Some of the recorded tumors have contained spicules of bone and calcareous material.



Fig 21-4 Fragments of tumor illustrated in Figure 21 2. Note that the tissue is firm and fibrous and the cortex is expanded, although it was intact.

Histopathology

A variety of histologic patterns have been described, but all of them are basically epithelial. There is variation from tumor to tumor and even within different fields of the same tumor A common pattern consists of masses of epithelial islands in which the peripheral cells, which are columnar are arranged in palisaded fashion In the centers of some of these islands a stellate reticulumlike appearance is observed. Even cyst formation may occur within these islands, and thus basic pattern has prompted use of the term adamantinoma. A second pattern consists of islands of cells that resemble cutaneous basal cells. As in the preceding type, these cellular aggregates often show peripheral palisading of nuclei, and they are ordinarily disposed in a fibrous stroma. The general appearance of this second type is very similar to that of basal cell carcinoma of the skin. Additional variation in the histopathologic appearance is afforded by fields that closely resemble squamous cell carcinoma and other fields that mimic ordinary adenocarcinoma.

It is obvious that the problem of differentiating adamantinoma from metastatic carcinoma may be difficult, especially if one considers only the histopathologic features.



Fig. 21 5 Multiple sections of the tumor illustrated in Figures 21 2 and 21-4 showed the pattern illustrated at the left (×200)

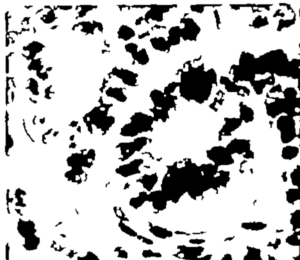


FIG 21-6. Part of the adamantinoma shown in Figure 21 3 had a glandular pattern, as shown at the right, whereas other zones resembled squamous cell carcinoma (×600) (Reproduced with permission from Dockerty M B. and Meyerding, H W., *J.A.M.A* 119 932 937 1942)

Treatment

After carefully reviewing all the recorded cases and amplifying the available information by sending questionnaires to the authors who reported the cases, Baker and his associates came to the conclusion that amputation is the treatment of choice. This conclusion was based upon the fact that in two thirds of the cases recurrence was known to have followed local excision, and recurrence was followed by death in eight instances.

One might be justifiably tempted to employ wide block excision of the involved segment of bone if the lesion is small and well located.

Prognosis

Early radical therapy should effect a high proportion of cures It is known, however, that temporizing with inadequate attempts at local excision has produced death in a number of patients, owing to metastasis.

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Chapter 22

Fibrosarcoma

FIBROSARCOMA occurring in bone is defined as a malignant tumor the spindle-shaped cells of which produce no osteoid material. Collagen production by the cells of these tumors varies from none to very marked. It seems unwise to exclude the group of spindle cell tumors that produce no collagen from the fibrosarcomas since they are merely at one end of the spectrum.

It is somewhat didactic to separate fibrosarcoma of bone from its close relative, fibroblastic osteogenic sarcoma. Relatively minor clinical features distinguish these two entities. Occasionally one finds osteoid substance only after prolonged search through many sections of a tumor that is predominantly fibroblastic, indicating that the separation is an artificial one The basic similarity of these neoplasms is further emphasized by the fact that both are best treated by ablative surgical means.

After exclusion of the tumors that merely abutted on bone, on the premise that they were very likely of soft-tissue origin, there remained in the Mayo Clinic series no distinct group of tumors that one might logically call "periosteal fibrosarcomas. This manner of selection perhaps excludes some sarcomas of periosteal origin. From the gross pathologic features it is apparent that most fibrosarcomas of bone arise in the medullary or the cortical regions, although some undoubtedly begin in the periosteum.

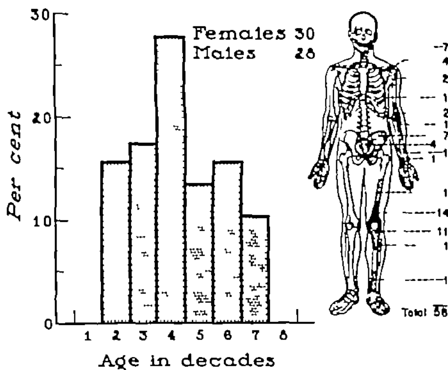


Fig. 21 Skeletal, age and sex distribution of fibrosarcoma.

Incidence

The 58 fibrosarcomas in this series comprised less than 4 per cent of the total primary malignant bone tumors. Fibrosarcoma was only one eighth as common as osteogenic sarcoma.

Sex

No sex predominance was evident in this relatively small series.

Age

The pure fibrosarcomas were rather evenly distributed among the second through the seventh decades of life. The tendency of fibrosarcoma to occur among older people as commonly as among the younger is the major clinical difference between it and osteogenic sarcoma.

Localization

The sites involved by pure fibrosarcoma do not differ remarkably from those involved by osteogenic sarcoma. The long bones are most commonly affected, and the tumor is usually found in the metaphyseal region. In the present series, seven fibrosarcomas were in the mandible, four in the scapula, two in the radius and one each in a rib, the lower portion of the ulna and the lower portion of the tibia.

Symptoms

Fibrosarcoma produces the ordinary symptoms of malignant tumor in bone, namely pain and swelling. In the average case these are of short duration. A small percentage of fibrosarcomas arise in benign neoplasms of bone, especially in giant cell tumors, and accordingly a history that the tumor has been present for a long time will ordinarily be elicited in such cases.

Physical Examination

Painful swelling in the region of the tumor is usually found unless the tumor is covered by a thick layer of uninvolved tissue.

Roentgenologic Features

As Pugh has so aptly stated, there are no roentgenologic features that distinguish fibrosarcoma of bone from osteolytic osteogenic sarcoma. The essential destructive characteristics of the latter tumor have been described previously. Periosteal, reactive new bone formation may be seen. There are no pathognomonic features of fibrosarcoma of bone, but in the average case the diagnosis of malignant tumor can be made with reasonable assurance.



FIG. — Fibrosarcoma producing irregular destruction of lower portion of femur. (Reproduced with permission from McLeod, J. J., Dahlin, D. C. and I[illegible], J. C. *Am J Surg* [In press] 19[illegible].)

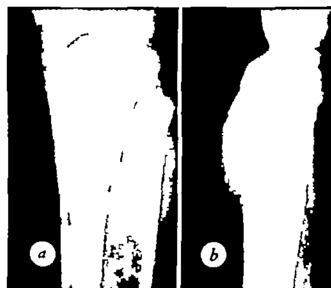


FIG. 22 3. Anteroposterior ( ) and lateral (*b*) views of fibrosarcoma of upper metaphyseal portion of tibia. Note the cortical destruction, especially anteriorly. (Reproduced with permission from McLeod, J. J., Dahlin, D. C. and Ivins, J. C.: *Am J Surg* [In press] 1957.)

Gross Pathology

Fibrosarcoma of bone may be composed of a firm, fibrous mass of tissue or of soft, fleshy friable tissue which invades the bone in an irregular fashion. Some tumors of this type, however are reasonably well circumscribed and can be shelled out of the bone of origin rather readily. Areas of necrosis and hemorrhage may be present. Almost all of the fibrosarcomas of central origin will have broken through the cortex and will present with a large or small extraosseous component. The average tumor of this type has its longest axis parallel to and within the bone of origin. Practically any bone and any portion of it can be affected by this neoplasm. In some instances the tumor is chiefly outside the bone and thus quite likely of periosteal origin.

Fibrosarcoma, like osteogenic sarcoma, metastasizes primarily by the hematogenous route, producing secondary deposits in the lung.



FIG. 22-4 Fibrosarcoma of lower portion of femur. This is the specimen from the case represented in Figure 22-2. (Reproduced with permission from McLeod, J. J., Dahlin, D. C. and Ivins, J. C.: *Am. J. Surg.* [In press] 1957.)



FIG. 22-5 Specimen from the case illustrated in Figure 22-3*a* and *b*. (Reproduced with permission from McLeod, J. J., Dahlin, D. C. and Ivins, J. C.: *Am. J. Surg.* [In press] 1957.)

Histopathology

Fibrosarcoma in bone has the same histologic features as its soft-tissue counterpart. Sections may, however, reveal that it is invading and destroying bone, especially near the periphery of the tumor. There is wide variation in the degree of differentiation of the component fibroblasts and in the amount of collagen produced. The nuclei vary from long and slender to oval in shape. Nuclear irregularities and the number of mitotic figures are increased in the more anaplastic (higher-grade) tumors. The collagen is arranged in rather orderly bands and whorls in the lower grade lesions. Some highly anaplastic spindle cell tumors produce no recognizable collagen, but such tumors are logically included among the fibrosarcomas because of their histologic kinship.

Benign multinucleated cells are sometimes found in fibrosarcomas, but they are more commonly seen among the malignant cells of osteogenic sarcomas.

Relatively few fibrosarcomas are so low grade that the problem of differentiation from benign lesions arises. The benign conditions that may enter into the problem of differentiation include cellular lesions of fibrous dysplasia and nonosteogenic fibroma of bone.



FIG 26 Grade 2 fibrosarcoma (×200) This section, which shows only slight collagen production, came from the tumor illustrated in Figures 22 3 and 22 5 *b* Periphery of fairly well-differentiated fibrosarcoma showing invading bone (×75) (Reproduced with permission from McLeod, J J, Dahlin, D C and Ivins, J C *Am J Surg* [In press] 1957)



FIG. 22 7 Relatively anaplastic fibrosarcoma with bizarre and irregular nuclei but with considerable collagen production (×100)

Treatment

Ablative surgical treatment of the type used for osteogenic sarcoma should be employed for fibrosarcoma of bone Details regarding management of tumors of various sites are given in Chapter 17 Fibrosarcoma is notoriously radioresistant.

Some have made a strong plea for conservative, block-excisional therapy for some of the well localized fibrosarcomas of long bones on the premise that they are relatively benign Experience at the Mayo Clinic indicates, however that fibrosarcoma is practically as lethal as osteogenic sarcoma and demands prompt, adequate therapy

Prognosis

Although 26.8 per cent of the patients in this series survived 5 years, more than one fourth of these survivors subsequently succumbed to the effects of their tumors

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Chapter 23

Chordoma

CHORDOMA is a neoplasm that develops from remnants of the primitive notochord. It apparently can arise from normal products of the notochord, the nuclei pulposi, or from abnormal "rests" of notochordal tissue. It ordinarily grows slowly and is malignant because of local invasion, but metastasis is distinctly uncommon.

Chordoma has a distinct predilection for the ends of the spinal column. Thus the sacrococcygeal region and the base of the skull in the vicinity of the spheno-occipital synchondrosis account for the great majority of cases. Small, nonneoplastic masses of vestigial notochordal tissue are not uncommonly found in the region of the spheno-occipital junction in the midline.

This tumor is relatively uncommon in the dorsal and lumbar portions of the vertebral column, which is strange in view of the fact that the largest masses of notochordal products, in the form of the nuclei pulposi, occur in these regions.

One might question whether chordoma is correctly classed among the neoplasms of bone. The intimate relationship of the notochord to the skeleton and the clinical and roentgenologic features of these tumors make the inclusion a logical one.

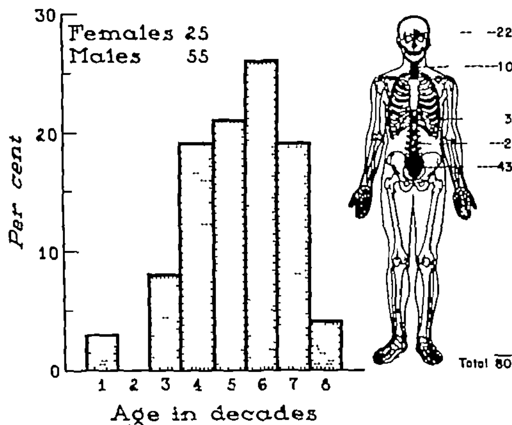


FIG. 23-1 Skeletal, age and sex distribution of chordoma

Incidence

Chordoma is usually referred to as a very rare neoplasm, but it accounted for almost 5 per cent of the malignant tumors in this series. Possibly a selection factor operates in a series such as this which includes many referred patients.

Sex

Chordoma affects males approximately twice as commonly as females.

Age

As indicated in the illustration above, chordoma is distinctly uncommon in patients less than 30 years of age. Two of the patients in this series were in the first decade of life and seven were in the third. Spheno-occipital chordomas are recognized clinically approximately a decade earlier in life than are those in the sacrococcygeal region.

Localization

Chordoma is so strictly localized to the midline regions of the body that this affords important diagnostic evidence. More than half the tumors occur in the sacrococcygeal region, and fully one fourth at the base of the brain. Most of the remainder involve the cervical vertebrae. The dorsal and lumbar vertebral regions are rarely affected.

Symptoms

The duration of symptoms prior to the time the patient seeks medical care varies from months to several years. Pain is a practically constant feature of sacrococcygeal chordoma, and characteristically it is located at the tip of the spinal column. Constipation owing to the presence of the tumor and complaints resulting from pressure on or destruction of nerves emerging from the distal portion of the spinal cord, may develop. In rare instances a sacrococcygeal chordoma produces a postsacral mass.

Spheno-occipital chordoma may cause symptoms referable to any of the cranial nerves, but those resulting from involvement of the nerves to the eye are by far the most common. This tumor may destroy the pituitary gland and produce evidence of its dysfunction, protrude laterally and give signs suggestive of a tumor of the cerebellopontine angle, or even erode inferiorly and obstruct the nasal passages. Large intracranial extension may evoke the general features of intracranial neoplasm.

Those chordomas that arise along the remainder of the spinal column most frequently produce symptoms that result from compression of nerve roots or the spinal cord.

Physical Findings

Almost every sacrococcygeal chordoma has a presacral extension that may be detected on careful rectal examination. The mass is, of course, firm and fixed to the sacrum. Digital and proctoscopic examination discloses that it is extrarectal Evidences of nerve dysfunction, such as cord bladder, anesthesias and paresthesias, are relatively unusual and late features.

Those chordomas that arise at the base of the brain may as already indicated, produce signs referable to any of the cranial nerves, or to involvement of the pituitary Examination of the visual fields may disclose defects that suggest the correct diagnosis. Only rarely does a patient complain of nasal obstruction.

Since chordoma of the cervical, thoracic and lumbar portions of the vertebral column may present posteriorly laterally or anteriorly a great variety of symptoms may be produced. For example, one in the cervical region of the spinal column may give clinical features that suggest the diagnosis of chronic retropharyngeal abscess. Most often, however physical examination discloses evidence of encroachment on the nerves or spinal cord.

Roentgenologic Features

Roentgenographic study reveals evidence of osseous involvement or a soft-tissue mass in more than 90 per cent of cases Seventy five per cent of sacrococcygeal examples are characterized by an irregular zone of destruction which begins in the midline of the sacrum. Residual osseous trabeculae and amorphous masses of calcification may be seen in the lesion. The sacrum is often expanded owing to the slow growth of the neoplasm A soft-tissue mass, almost always anterior is usually visible.

Cranial chordoma nearly always produces roentgenographic changes but rarely contains radiopaque masses Destruction of bone in the spheno-occipital or hypophyseal region is usually evident. Some portion

of the sella turcica is affected in the majority of cases Invasion and destruction of the sphenoid and petrous bones are occasionally seen. Ventriculography and cerebral angiography may aid in localizing the lesion.

The chordomas that involve the cervical, thoracic and lumbar segments of the spinal column usually produce significant roentgenographic changes. Zones of bone destruction, sometimes containing dense foci, are seen involving one or more vertebrae. Some of these tumors, especially if they displace the pharynx or trachea, produce a significant soft tissue mass.



Fig 23-2. Destruction of sacrum and coccyx by chordoma that has also produced large soft-tissue mass in the pelvis. (Reproduced with permission from Utne J R and Pugh, D G *Am J Roentgenol* 74 593-608, 1955)



FIG. 23-3 Marked involvement in the region of the sella by chordoma of the spheno-occipital zone. (Reproduced with permission from Dahlin, D. C. and MacCarty, C. S. *Cancer* 5:1170-1178, 1952.)





FIG. 23-4 Lateral view of surgically excised chordoma. There is expansion of the sacral cortex by an antesacral soft tissue mass. *b* Lateral view of the cervical segment of the spinal column demonstrating the soft-tissue shadow of a cervical chordoma anterior to the third, fourth and fifth cervical vertebrae. (Reproduced with permission from Utne, J. R. and Pugh, D. G. *Am. J. Roentgenol.*, 74:593-608, 1955.)

Gross Pathology

A chordoma is a soft, lobulated grayish tumor that is semitranslucent and resembles chondrosarcoma or even mucous adenocarcinoma It is usually well encapsulated except in the region of bone invasion, where no distinct edge of the tumor may be delineated Sacral chordoma practically always has a presacral extension that is usually covered by the elevated periosteum. It may extend into the spinal canal. A spheno-occipital chordoma almost always bulges into the cranial cavity and distorts or destroys structures at the base of the brain

Sometimes chordoma at the base of the brain penetrates into and fills the sphenoid sinus or even the nasal or nasopharyngeal cavities. From any of these sites material may be readily removed for biopsy

Although it has been stated frequently that 10 per cent of chordomas metastasize this figure does not withstand critical analysis. Hematogenous metastasis does occur on rare occasions, however and the present series of 80 cases contains one proved example

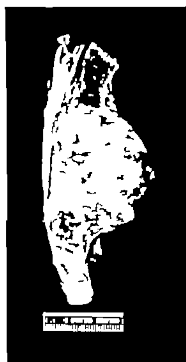


Fig 23-5 Sacral chordoma with anterior extension. This is the smallest surgically excised tumor of this region in the present series (Reproduced with permission from Dahlin, D C. and MacCarty C S *Cancer* 5 1170-1178, 1952)



Fig 23-6. Spheno-occipital chordoma removed at necropsy Note the mass posterior to the region of the optic nerves, the carotid vessels and the pituitary body



FIG. 23-7 Sacral chordoma more than 10 cm. in diameter. This specimen shows the lobular feature of chordoma especially well.

Histopathology

Chordoma cells are characteristically disposed in lobules. Physaliferous cells that are vacuolated because of intracytoplasmic, mucous droplets are usually described as characteristic of chordoma, and they can be found in most of these tumors. Sometimes, however they are present in only small numbers and constitute an insignificant portion of the histologic picture. The intracellular vacuoles, when they are present vary in size from those that are barely visible to those that are several times the diameter of the cell's nucleus. Syncytial strands of cells lying in a mass of mucus that has no doubt been formed by the cells are almost as characteristic as are the physaliferous cells. Cell boundaries in these syncytial strands are indistinct.

Considerable variation of nuclear size and chromatin is seen in some of these tumors and mitotic figures may also be present. Such evidences of cellular activity did not alter the clinical course of the sacrococcygeal chordomas in the present series.

Special stains have been of no real value in diagnosis of this tumor. Chordoma cells often give a positive reaction to glycogen stains but a similar type of reaction is observed in chondrosarcoma, one of the two tumors that offer a differential diagnostic problem. Mucous stains are likewise of little value because the other differential diagnostic problem, mucous adenocarcinoma, as well as chordoma, produces mucicarmine positive material.

Chordoma that arises in the spheno-occipital region is sometimes differentiated from chondrosarcoma only with great difficulty.



FIG. 3-8 Periphery of chordoma to show characteristic lobular pattern seen in these tumors (×30) (Reproduced with permission from Dahlin, D. C. and MacCarty, C. S. *Cancer* 5:1170-1178, 1952.)





FIG. 23-9 Mucous vacuoles in the cytoplasm of chordoma cells, the so-called physaliferous cells (×100). *b* Syncytial strands of cells in a sea of mucus, a very common pattern in chordoma (×100). (Reproduced with permission from Dahlin, D. C. and MacCarty, C. S. *Cancer* 5:1170-1178, 1952.)



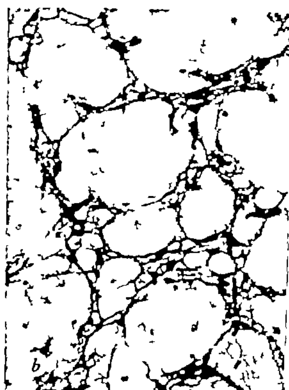


FIG 23-10 *a* Cells with scanty eosinophilic cytoplasm and indistinct cell boundaries lying in mass of mucus (×325) This is a common finding in chordoma *b* Physaliferous cells arranged in strands separated by mucus (×205) This is another of the patterns produced in chordoma.



FIG. 23-11 Nuclear abnormalities and even fairly abundant mitotic figures are seen in minority of chordomas (×100) (Reproduced with permission from Dahlin, D C. and MacCarty C. S *Cancer* 5 1170-1178, 1952.)

Treatment

Until recently the treatment of chordoma was quite unsatisfactory. The tumor was only partially removed and the patient was afforded palliative benefit at best. The only cheerful aspects were that, owing to the slow growth of the tumor, a few patients obtained several years of freedom of symptoms after subtotal removal and some chordomas proved to be radiosensitive.

It has now been established that radical, complete removal of some sacrococcygeal tumors is feasible and should be attempted. The plane of excision must be well beyond the edge of the tumor to avoid recurrence due to implantation. For those tumors not amenable to radical removal and for inoperable recurrent lesions after surgical therapy, radiation should be employed.

Many surgeons feel that spheno-occipital chordomas are so inaccessible that complete removal is practically always impossible even when they are first seen, and that radiation is the treatment of choice. When a chordoma in this location produces increased intracranial pressure, however, surgical intervention may be necessary.

Prognosis

Prior to adoption of the more radical surgical technic, even the patient with sacrococcygeal chordoma was doomed to eventual, though perhaps delayed, death from local extension of the tumor. The sacrococcygeal neoplasm often extended to block the genito-urinary or gastrointestinal tract, and the spheno-occipital tumor produced lethal intracranial complications. Subtotal surgical removal or radiation may produce gratifying remissions.

Radical surgical technics will no doubt afford permanent cure for some of the less extensive sacrococcygeal chordomas. It must be remembered, however, that this tumor usually grows slowly and that long-term follow-up is necessary in the evaluation of any therapeutic regimen.

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Chapter 24

Conditions That Commonly Simulate Primary Tumors of Bone

Metastatic Carcinoma

METASTATIC DEPOSITS from carcinomas are by far the most common malignant tumors affecting the skeleton. Although the correct diagnosis is usually obvious when the clinical history is considered, it is often unsafe to assume that any given skeletal lesion or lesions are necessarily related to a proved carcinoma. The punched-out areas of destruction characteristic of myeloma, for example, may be mistaken for areas of lytic metastatic deposit. Metastatic carcinoma is especially likely to afford a diagnostic problem when only one skeletal lesion is found and no "primary" is known. A destructive process secondary to hypernephroma is particularly prone to simulate a primary lesion of bone, because this cancer has a tendency to produce a clinically solitary metastatic lesion and the primary tumor is in an obscure location. Carcinomas may invade bone by direct extension.

Metastatic carcinoma affects chiefly the older age groups. It is especially prone to involve the vertebral column, the pelvis, the ribs, the calvarium, and even the large bones of the limbs near the body. Metastasis *of carcinoma distal to the levels of the knees and elbows, however, is uncommon.*

Clinically the osseous lesions of metastatic carcinoma may closely simulate primary malignant tumor. Pain, with or without swelling, and symptoms resulting from pressure on neighboring structures or from pathologic fracture are the most prominent.

Roentgenologically metastatic tumors usually produce irregular destruction of bone indicative of their malignant quality. Although most such lesions are osteolytic, many metastatic deposits from carcinoma of the prostate and some of those from other tumors are osteoblastic. Even malignant lymphomas sometimes evoke considerable sclerosis. Occasionally, especially in the pelvic bones, broadening of the osseous outline may result from periosteal elevation by the growing tumor and subperiosteal formation of new bone. The region of actual involvement by metastatic carcinoma is frequently more extensive than is seen roentgenographically.

Pathologically the lesions of metastatic carcinoma in bone do not present diagnostic characteristics from the gross standpoint. Lesions vary from those that are fibrotic owing to scirrhous reaction produced by the tumor to those that are extremely soft and mushy. The osteoblastic metastatic lesions so often seen from prostatic carcinoma are very dense and relatively characteristic. Histologically the average metastatic carcinoma to bone with its glandular or squamous elements is readily diagnosed. Even if these are absent the characteristic pattern of small islands of epithelial cells interspersed within a fibrous stroma are

pathognomonic Some highly anaplastic carcinomas with spindling nuclei closely simulate fibrosarcoma. In such instances, when one encounters a single metastatic lesion from a hidden primary it may be extremely difficult to decide whether one is dealing with a primary malignant tumor This is especially true of certain hypernephromas

The *treatment* of patients with skeletal metastasis is becoming increasingly important Certain carcinomas, especially those from the prostate and breast, are benefited by both medical and surgical hormonal therapy Carcinoma, metastatic from the thyroid, may be held in abeyance for protracted periods by the use of radioactive iodine Orthopedic surgical procedures in combination with radiation or other therapy are often of much value in the management of metastatic carcinoma to the skeleton. Amputation for solitary skeletal metastatic lesions must occasionally be considered. In the present series there is a case in which a solitary metastatic deposit developed in the distal part of the femur 8 years after removal of a hypernephroma, and amputation was followed by known survival for 11 additional years.

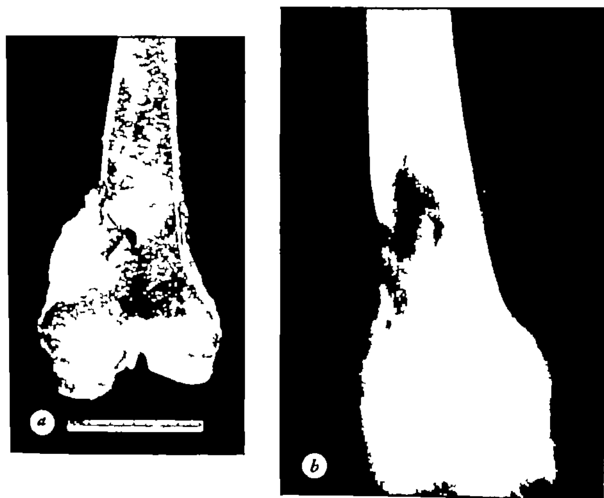


FIG 24-1 Gross specimen and, *b* roentgenogram of metastatic squamous cell carcinoma, grade 1 This lesion developed 10 years after below knee amputation for a grade 1 squamous cell carcinoma of the foot. Popliteal lymph nodes were uninvolved and the pathogenesis of this metastatic lesion is obscure.



Fig. 24-2 Slightly expansile metastatic hypernephroma of neck of scapula. The renal tumor had been removed 6 years previously and for 18 months the patient had had shoulder pain. The scapular lesion was given radiation therapy and when no other foci appeared, scapulectomy was performed and the patient was well more than 1 year later.



Fig. 24-3 Typical metastatic hypernephroma with clear cells in an organoid pattern (×150)



FIG. 24-4. Extensive lytic carcinomatous deposits secondary to a primary lesion in the breast. (Reproduced with permission from Pugh, D. G. *Roentgenologic Diagnosis of Diseases of Bones*. Baltimore, Williams & Wilkins, 1954.)

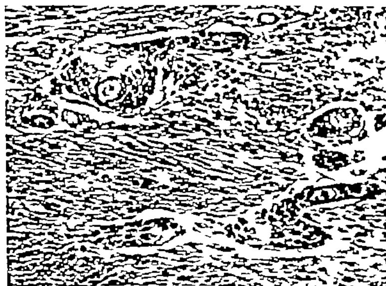


FIG. 24-5. Nests of cells of metastatic squamous cell carcinoma in the skeleton. Note the extensive fibrogenic reaction and the clusters of lymphocytes. (×150)

Fibrous Dysplasia

Fibrous dysplasia is probably the result of an anomaly in the development of bone. It is characterized by the occurrence of one, a few or numerous discrete skeletal defects. Yellow or brown patches of cutaneous pigmentation may accompany the bone lesions especially in patients with a severe disseminated form of the disease. When, in addition to cutaneous pigmentation, such polyostotic disease is accompanied by signs of endocrine abnormality especially precocious puberty in girls, the condition is commonly called "Albright's syndrome."

"Fibro-osseous dysplasia" is a term that is gaining acceptance for many of the defects of this type that involve the base of the skull and the jawbones Dysplastic lesions at these sites often contain such an abundance of osseous trabeculae intermingled with the fibrous tissue that they are distinctly hard and may cast a dense shadow in the roentgenogram. Many if not all, of the so-called osteofibromas and fibro-osteomas in these locations are actually examples of fibro-osseous dysplasia.

Polyostotic fibrous dysplasia usually manifests itself early in life, as does also the monostotic form. The disease is relatively common, Pritchard being able to review 236 cases from the literature in 1951 Almost any bone in the body may be affected, and those lesions in the jawbones or at the base of the brain are especially likely to come to clinical and surgical attention.

Clinically many of the lesions of fibrous dysplasia are completely asymptomatic and never discovered, as evidenced by the finding of occasional "silent" lesions in x ray examination of the thorax. The dysplasia may produce defective growth and deformity of a long tubular bone. Those lesions that involve the bones of the face and skull usually produce signs and symptoms because of their size, such as focal swelling and exophthalmos. Deformity due to the mass is the usual problem presented by patients with lesions in the jaws.

Roentgenologically the defects of fibrous dysplasia are usually well-defined zones of rarefaction. Expansion with thinning of the cortex is especially likely to occur in narrow bones such as the ribs. Those lesions with a large osseous component such as are commonly seen around the base of the skull and the maxilla are likely to be relatively radiopaque. This characteristic is accentuated if the lesion bulges into an air-containing sinus.

Grossly examination reveals considerable variation in the lesions of fibrous dysplasia, but the average one is well defined and composed of dense, whorled, fibrous tissue Embedded in this fibrous tissue there are usually enough small osteoid trabeculae to impart a distinctly gritty quality Slight to extensive cyst formation may be present, whereas those with marked ossification may resemble osteoma. Those lesions that arise from thin bones such as the maxilla may bulge into adjacent cavities or soft-tissue zones in a polypoid fashion

Microscopically the major feature is proliferating fibroblastic connective tissue. This tissue in itself is nonspecific unless it contains zones with irregular trabeculae of osteoid or bone. These trabeculae have a

completely meaningless arrangement as regards function. Metaplastic chondroid substance is sometimes present and on rare occasions it is so prominent that the question of a neoplasm of hyaline cartilage arises. Areas of degeneration may contain only relatively acellular fibrous tissue which is not diagnostic of fibrous dysplasia. Some are composed predominantly of osteoid and bone with only sparse fibroblastic elements separating the trabeculae. Sometimes, especially in lesions of the jaws and at the base of the brain, the osseous component is in the form of little spherical masses which are surrounded by the proliferating spindle cells in such a fashion that psammomatous meningioma is simulated. Mitotic figures are found in the actively proliferating lesions of fibrous dysplasia.

Treatment should be conservative. The lesions commonly stop growing at puberty. Therapy should be directed at restoring the normal configuration when the skull or jawbones are affected. In long bones, deformity secondary to the disease may require correction. Radiation therapy is probably of no value and, in a few recorded cases, sarcomatous transformation has followed its use.

The *prognosis* in fibrous dysplasia is generally good. The deforming lesions of the jawbones or skull may sometimes recur but ordinarily they respond favorably to additional conservative surgical therapy. In rare instances polyostotic fibrous dysplasia produces such marked deformity of bones of the extremities that amputation becomes necessary.



FIG. 24-6 *a* Fibrous dysplasia producing expansion of several centimeters of right eleventh rib. *b* Polyostotic fibrous dysplasia producing marked deformity of leg.



Fig. 24-7 Fibrous dysplasia causing pronounced distortion of base of skull and periorbital regions. Grossly this lesion was partially cystic.

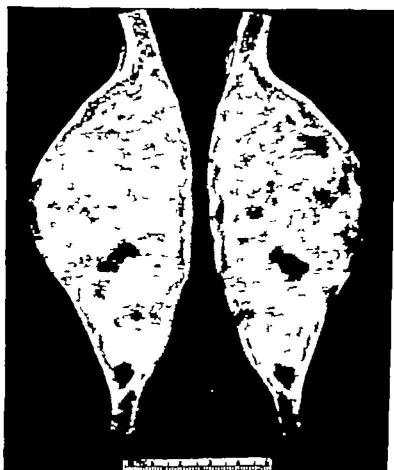


Fig. 4-8 Longitudinal section of rib expanded by fibrous dysplasia. (Reproduced with permission from Zimmer, J. F., Dahlin, D. C., Pugh, D. G. and Clagett, O. T.: *J. Thoracic Surg.* 31:488-496, 1956.)





Fig. 24-9 *a*. Classic fibrous dysplasia with proliferating fibroblastic tissue and bizarre masses and trabeculae of osteoid tissue and bone (×75) *b*. Fibro-osseous dysplasia, in this instance producing spherical masses of osseous tissue. This pattern is often seen in lesions at the base of the skull and has been mistaken for meningioma (×100)



Fig. 24-10 Chondroid zones such as this are not uncommon in lesions of fibrous dysplasia and, in rare instances, they dominate the histologic picture (×85)

Aneurysmal Bone Cyst

Aneurysmal bone cyst is one of the "variants" that has been justifiably excluded from the bona fide giant cell tumors. Features that make it logical to exclude this lesion from the neoplastic category include the observation that examples of it have regressed following incomplete removal. The cause of this strange process in bone is unknown.

In the present series, aneurysmal bone cyst has been less than half as common as giant cell tumor of bone. No distinct sex predilection has been observed in reported cases. Two thirds of the affected patients are less than 20 years of age, which is in striking contrast to the age distribution of true giant cell tumors, 90 per cent of which occur in patients 20 years of age or older. Although aneurysmal bone cyst has been seen most commonly in the long bones, where it has a predilection for the metaphyseal region, almost any bone of the body may be affected.

Clinically pain and swelling are the important features and they vary in duration from weeks to a few years. The lesion tends to increase in size until therapy is instituted. Vertebrae are relatively commonly involved, with the production of signs and symptoms owing to compression of the spinal cord and emerging nerves.

Roentgenographically the lesion often has a characteristic appearance. A zone of rarefaction, which is usually well circumscribed and eccentric, is associated with an obvious soft-tissue extension of the process. In the classic case this soft-tissue extension is produced by bulging of the periosteum and a resultant layer of roentgenologically visible new bone which delimits the periphery of the tumor. The lesional area tends to show trabeculation. Fusiform expansion may be produced when small bones such as a rib or a fibula are affected.

Grossly an aneurysmal bone cyst contains anastomosing cavernomatous spaces which ordinarily comprise the bulk of the lesion. The spaces are filled with unclotted blood. Blood wells up into, but does not spurt from, the tumor when it is unroofed. The egg-shell thick layer of subperiosteal new bone which delimits the lesion is ordinarily readily discernible. Some of these lesions contain solid fleshy and friable or fibrous and granular zones which may comprise half of their bulk.

Microscopically the essential feature is the presence of cavernomatous spaces, the walls of which lack the normal features of blood vessels. Thin strands of bone are often present in the fibrous tissue of these walls. An endothelial lining is unusual. Reconstruction of these cavernomatous spaces from curetted fragments may be extremely difficult. The solid portions of an aneurysmal bone cyst may be fibrous but they ordinarily contain a lacework of osteoid trabeculae similar to that observed in giant osteoid osteoma. Benign giant cells are often present in large numbers thus accounting for the confusion of this lesion with genuine giant cell tumor. These solid zones with giant cells may resemble giant cell reparative granuloma of jaw bones.

The most successful *treatment* has been surgical removal of the entire lesion or as much of it as possible. Occasionally bone grafting of the resultant defect may be necessary. Rarely an aneurysmal bone cyst recurs when it is incompletely removed. Malignant transformation has been reported in only two instances, in both of which radiation therapy was employed.



FIG. 24-11 Classic aneurysmal bone cyst of second cervical vertebra (Reproduced with permission from Dahlin, D C., Besse, B. E., J Pugh, D G and Ghormley R K. *Radiology* 64:56-63 1955)



FIG. 24-12. Another typical example, here affecting the ulna. (Reproduced with permission from Besse, B. E., J Dahlin, D C., Pugh, D G and Ghormley R. K. *Clin Orthopaedics* 7 93-102, 1956.)



FIG 24-13 This aneurysmal bone cyst of the tibia had not yet produced much expansion.





Fig. 24-14 *a* and *b*. Aneurysmal bone cyst of mandible. This lesion had produced swelling for 3 months and had recurred after incomplete removal. Wide excision with preservation of the mandible resulted in cure.

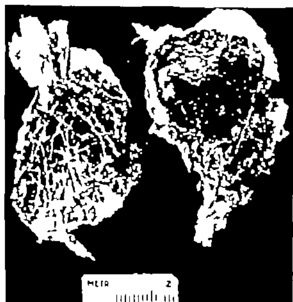


Fig. 24-15. Surfaces produced by sagittal section of aneurysmal bone cyst of upper portion of fibula. (Reproduced with permission from Dahlin, D. C., Besse, B. E., Jr., Pugh, D. G., and Ghormley, R. K.: *Radiology* 64:56-65, 1955.)



Fig. 24-16. Specimen from mandible of patient illustrated in Figure 24-14. Portions of this aneurysmal bone cyst exhibited the features of giant cell reparative granuloma.









FIG. 24-17 *a* Portion of the wall of a large cavernomatous space, showing that a smaller blood space is present in the wall (×40) *b* Thicker and more cellular walls of blood spaces, here containing a few giant cells (×55) *c* Solid portion of aneurysmal bone cyst, here containing osteoid trabeculae and numerous benign giant cells (×80) *d* Solid fibrous area with cavernous space on right (×65) (Figure 24-17*b* and *d* reproduced with permission from Dahlin, D C., Besse B E., Jr Pugh, D G and Ghormley R. K.: *Radiology* 64 56-65 1955)

Myositis Ossificans

Myositis ossificans is a benign process which in its early or "florid" phase presents such marked cellular activity that it may be mistaken for sarcoma. The lesions of this troublesome disease are rarely explored surgically in their "florid" stage, so that they are not commonly encountered. The relative rarity of this disease, however, has delayed understanding of the peculiar tissue reaction associated with it.

Clinically the patient may or may not have experienced significant recent trauma. Sometimes there is a history of unusual muscular exertion. A mass is present in most patients treated surgically. The mass commonly develops in as short a time as a week or two and sometimes it recurs just as rapidly after surgical removal. This rate of development affords a diagnostic clue, since sarcomas rarely grow so fast.

Roentgenographically in the earliest stages it may show no evidence of calcific substance. Usually, however, there is a more or less well-circumscribed, partially osseous tumor which may give the false appearance of being attached to bone when viewed with only one projection. Some of the deeper lying tumors may abut on the cortex of a bone and even be associated with some periosteal reaction. Ordinarily, however, stereoscopic studies reveal that the bone's cortex is not involved, a feature that aids materially in the differentiation from osteogenic sarcoma. With progression of the lesion, increased ossification develops until finally it is obvious roentgenologically that the process is benign.

Grossly the tumor is well circumscribed except in the very early phases. It may be completely contained in the belly of a muscle, although an entirely similar process sometimes develops with no apparent relationship to a muscle. It is usually obvious that the lesion did not arise in bone. Ossification is characteristically most pronounced at the periphery of the mass. The central portion may contain small cysts.

Microscopically active fibroblastic proliferation is the dominant feature and mitotic figures may be numerous. In all but the earliest lesions of this type, evidence that the fibroblasts are undergoing metaplasia to osteoblasts is present. These osteoblasts produce strands of new osteoid tissue that rapidly become well-formed osseous trabeculae. These are disposed in a somewhat parallel fashion that simulates the appearance of a callus. This "functional" arrangement of the osteoid and osseous trabecula, combined with the lack of true anaplasia in the proliferating cells, affords the histopathologist with the necessary diagnostic clues for the exclusion of sarcoma. Sometimes a chondroid phase is interposed between that of the proliferating fibroblasts and that of the osseous trabecula.

Treatment is usually unnecessary if one knows the correct diagnosis.

The *prognosis* is good whether the lesion is excised or amputation is performed because of an erroneous diagnosis. As indicated, sometimes the tumor recurs rather rapidly following excision, but such recurrences are, likewise, benign.

A few instances of malignant transformation of myositis ossificans have been recorded, but it is difficult to assess the authenticity of such cases.



FIG. 24-18. Myositis ossificans. The patient had had local pain for 1 month. It began after strenuous gymnastics.





FIG. 24-19. *a* Actively proliferating fibroblasts with mitotic figure in early lesion of myositis ossificans. Note that the nuclei do not appear anaplastic (×520). *b* Here the fibroblasts have undergone metaplasia and are producing more or less parallel strands of bone (×45).

Simple Cyst

Simple or "unicameral" cyst of bone is of unknown cause but apparently results from a disturbance of growth at the epiphyseal line. It is relatively common and usually becomes manifest during the first two decades of life. In most cases it occurs in the upper part of the diaphysis of the humerus, the diaphysis of the femur, or the proximal part of the diaphysis of the tibia, in that order of frequency.

Clinically the patient with a simple cyst of bone may have local pain, but in most cases the cyst comes to attention only after pathologic fracture has occurred. Occasionally there is swelling in the region.

Roentgenologically there is often fusiform widening of the bone due to slight expansion in the cystic zone. *The cortex is ordinarily eroded and thinned but it is intact unless pathologic fracture has occurred.* Fine trabeculation through the lesion is sometimes seen, and a healed fracture may be evident as a partition through it. A simple cyst usually reaches maximal size before the patient has matured. Frequently serial roentgenograms reveal that the epiphysis grows away from the region of the cyst so that it lies near the center of the shaft. A cyst not abutting on the epiphysis is referred to as a latent one.

Grossly the cystic cavity may contain nothing, but is usually filled with a clear or yellowish green fluid of low viscosity. The inner surface of the cyst wall frequently displays ridges separating depressed zones, and sometimes it is covered by a layer of fleshy tissue a centimeter or more in thickness. Not infrequently partial or complete septa are seen, the latter type making the cyst multicameral. Recent or old fractures produce modifications of this picture.

Histologically the lining of the cyst may be merely a very thin layer of fibrous tissue. Thicker areas when present are composed of fibrogenic connective tissue which often contains numerous benign giant cells, hemosiderin pigment, a few chronic inflammatory cells, and lipophages. Because of their giant cell component some of these lesions have been erroneously classed with giant cell tumors. Individual septa, when present, resemble closely those seen in typical aneurysmal bone cyst. The histologic as well as the gross features may have been modified by fracture.

Treatment when necessary consists of curettage of the walls of the cyst with complete evacuation of its contents. Bone chips are ordinarily employed to fill the defect. It is difficult to determine the optimal time for treatment. A recurrence rate of approximately 50 per cent can be expected if the patient is less than 10 years of age when the cyst is usually juxta-epiphyseal in location. The chance for permanent cure is good in patients that are more than 10 years of age, when the cyst ordinarily has been left behind by the growing epiphyseal line.



Fig. 4-20 (*above*). Inner surface of simple cyst of upper end of fibula. Note the ridges separating depressed areas.



Fig. 4-21 (*above right*). Classic appearance of simple cyst of upper portion of shaft of humerus. Fracture had occurred.

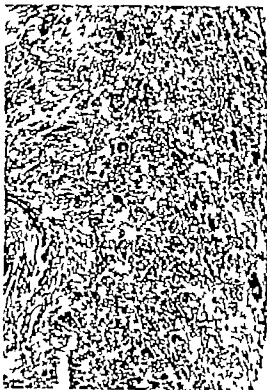


Fig. 24-22 (*right*). Lining of simple cyst. In this case there is a thick layer of fibrous tissue, along with fairly numerous benign giant cells (×100)

Osteomyelitis

The alterations of bone that result from acute or chronic infection may produce roentgenographic changes that simulate those of bone tumors. Antimicrobial therapy sometimes attenuates the infection to such a degree that normal roentgenographic progression is distorted, thus increasing the likelihood of mistaking an infection of bone for a neoplasm.

Clinically the febrile and septic course of acute osteomyelitis is sometimes obscured by therapy. Furthermore, some of the neoplasms, notably Ewing's sarcoma, produce fever and leukocytosis.

Roentgenologically the earliest sign of osteomyelitis is irregular rarefaction, usually near the end of the shaft of a long bone. Periosteal elevation commonly occurs and one or more layers of subperiosteal new bone may be produced. Islands of dead bone which develop later are relatively radiopaque owing to the osteoporosis that occurs in the surrounding living bone. On occasion the roentgenographic shadow may simulate exactly that produced by a malignant bone tumor. Sometimes, specific chronic infections such as tuberculosis and brucellosis produce a discretely demarcated zone of bone destruction that resembles that produced by a slowly growing benign tumor of bone. At other times a large zone of sclerosis results from an indolent focus of infection in bone and such a lesion can mimic the appearance of an osteoid osteoma in which the nidus is obscure.

Grossly the granulation tissue present at the site of osteomyelitis may not be identifiable as nonneoplastic.

Microscopically the differentiation from neoplasm is usually readily apparent. The granulation tissue characteristically contains numerous newly formed capillaries and an admixture of polymorphonuclear leukocytes, plasma cells and lymphocytes in varying proportions. On some occasions, when almost a pure plasma cell reaction is evoked, the histologic pattern bears a resemblance to that of multiple myeloma. Ordinarily, however, the network of proliferating capillaries produces the unmistakable pattern one associates with reaction to infection.

The *treatment* of osteomyelitis varies with the organism responsible for the infection. Management of the condition is sometimes greatly facilitated by examination of fresh frozen sections at the time of operation. In certain specific mycotic infections, for instance, the diagnosis can be made or strongly suspected from the histologic appearance. Whenever the histologic pattern is that of a granulomatous type of inflammation, bacteriologic investigation can be appropriately directed.



FIG. 24-23 Osteomyelitis of humerus. This occurred in a 9-year-old boy who had noted local pain for 1 month. The cultures from the lesion revealed Micrococcus pyogenes.

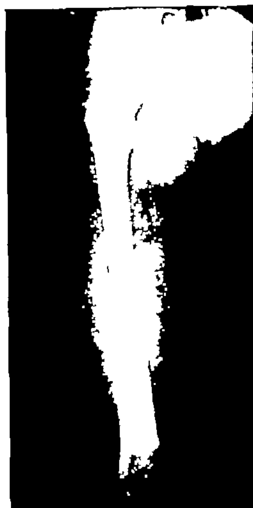


FIG. 24-24. Another osteomyelitic lesion that roentgenologically simulates sarcoma. This, like the one shown in Figure 24-23, was caused by M. pyogenes and had destroyed bone and caused periosteal formation of new bone.

Epidermoid Cyst

Islands of squamous epithelium sometimes become embedded in bone and, with continued slow growth, a markedly expansile lesion may be produced. Almost all such cysts occur in the bones of the face and skull. In addition to causing expansion of the affected bone the cyst may protrude and displace adjacent soft tissue. Accordingly some of them, especially if they are in roentgenologically obscure locations, may have the clinical features of tumors arising in the brain. Sometimes an epidermoid cyst is dumbbell shaped and protrudes beyond both the inner and outer tables of the skull.

Roentgenologically the rarefied defect in bone produced by an epidermoid cyst is typically very sharply defined and surrounded by a thin layer of sclerotic bone.

Grossly epidermoid cysts are usually filled with a pearly white mass of inspissated, keratinized squamous epithelium. The microscopic diagnosis depends upon demonstration of a squamous epithelial lining in at least some portion of the cyst wall.



FIG. 4-5 Large epidermoid cyst of skull. It had produced mass that bulged into the cranial cavity and outwardly as well.

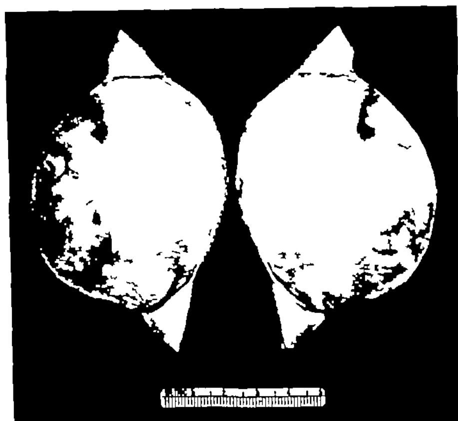


Fig 24-26. Epidermoid cyst shown in Figure 24-25. It was excised in its entirety. Since the contents were very soft, the mass was frozen before it was cut for this picture. It bulges internally more than externally.

Histiocytosis X (Reticuloendotheliosis)

This category includes a spectrum of conditions that range from the usually solitary and curable eosinophilic granuloma through the disseminated process that produces the Schüller-Christian syndrome to the fulminating rapidly fatal variety known as Letterer-Siwe disease. Osseous lesions ordinarily dominate the pathologic picture of histiocytosis x, it being basically a disease of the reticulo-endothelial system.

Letterer Siwe s syndrome usually affects very young children, whereas the Schüller-Christian syndrome and eosinophilic granuloma are seen most often in children and young adults. Practically any bone of the body may be affected, but there is a predilection for the skull

A great variety of *symptoms* is produced. Ordinarily patients with eosinophilic granuloma have a solitary painful focus The triad of the Schüller-Christian syndrome classically includes exophthalmos, often unilateral, diabetes insipidus and rarefied defects of bones of the skull. A partial triad, however has the same serious prognosis if other evidences of dissemination such as anemia, splenomegaly fatigability weight loss and lymphadenopathy are present. Patients with histiocytosis x may complain of discharge from the ears owing to involvement of the temporal bones, loosening or falling-out of the teeth secondary to lesions of the jaw and any of the symptoms that might be produced by focal destruction of bone. Any bone may be the site of a painful and sometimes expansile lesion. Vertebral involvement may result in collapse of a vertebral body with resultant neurologic symptoms Cutaneous manifestations, lymphadenopathy and splenomegaly are most common in the highly fatal Letterer Siwe variant. Pulmonary infiltration may become clinically important and, on rare occasions, it is the only significant evidence of the disease.

Roentgenologically the defects in bone are usually discretely defined. Periosteal reaction may be present when the cortex becomes eroded or when pathologic fracture has occurred. In the case of solitary lesions such reaction combined with a poorly defined zone of rarefaction may produce a shadow like that of a malignant bone tumor Multiple adjacent defects often become confluent. Lesions in the mandible are usually concentrated along the alveolar process. The teeth, in consequence may appear to have no bony support, which indeed is the case

Grossly the lesional tissue is soft It may be gray pink or yellow

The *microscopic appearance* is what links these three general conditions together The salient and pathognomonic feature consists of foci of proliferating histiocytic cells. These histiocytes frequently have ill-defined cytoplasmic boundaries and characteristically contain an oval or indented nucleus. Multinucleated histiocytes may be seen Although chromatin clumping and nucleoli are inconspicuous, mitotic figures are not uncommon This has led to the confusion of histiocytosis x with malignant tumors on some occasions. Zones of necrosis are present in considerable number The histiocytes may be swollen owing to cholesterol in their cytoplasm An ulcerated lesion of histiocytosis x may have its histologic features obscured by secondary inflammation

The *treatment* of lesions seen in eosinophilic granuloma and in the Schuller-Christian syndrome is roentgen therapy in moderate dosage. The diffuseness of the lesions in the fulminating Letterer Siwe syndrome usually precludes satisfactory therapy

Complete evaluation of patients who present with a defect characteristic of histiocytosis x is important in estimating *prognosis* Those patients who have only one or a few lesions are usually cured by local roentgen therapy Patients with the Schüller-Christian type of disease have a poor long-term outlook, but prolonged palliation can be expected if roentgen therapy is administered judiciously Patients with Letterer Siwe disease ordinarily succumb in a matter of months.

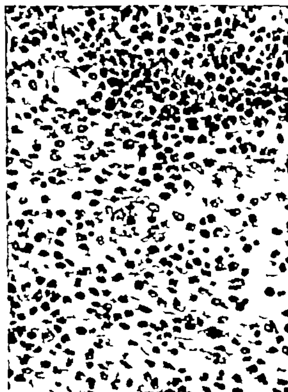




FIG. 24-27 (*above*) Lesion of histiocytosis x showing essential pale-staining histiocytes and darker eosinophils which commonly accompany the basic cells of the lesion (×385)

FIG. 24-28 (*above right*) Higher magnification to illustrate details of histiocytes. Note mitotic figure near center of field (×1000)



FIG. 24-29 (*right*) Skull defect produced by histiocytosis x The skull is one of the commonest sites for lesions in this disease

Giant Cell Reparative Granuloma

This lesion is peculiar to the jawbones. It has been commonly confused with genuine benign giant cell tumor of bone. The concept that it is not a neoplasm but rather some peculiar reactive lesion is gaining acceptance. The lesion consists of proliferating fibroblasts and, often, zones in which metaplasia is resulting in the formation of orderly osseous trabeculae. A variable amount of vascularity and microcyst formation may be seen. The basically fibrogenic quality of the lesional tissue is the main feature that differentiates giant cell reparative granuloma from true giant cell tumor. Actually, true giant cell tumors are found extremely rarely in the jawbones. The differentiation of these two lesions is important. Complete removal of giant cell reparative granuloma almost always effects cure, whereas true giant cell tumors recur in 50 per cent of cases and 10 per cent of them become malignant. Giant cell reparative granuloma commonly occurs in persons in the first decade or two of life as well as in older people.

There appears to be little difference between the lesions within bone that present the histologic characteristics of giant cell reparative granuloma and those that are basically soft-tissue tumors of the gums with little or no osseous involvement.

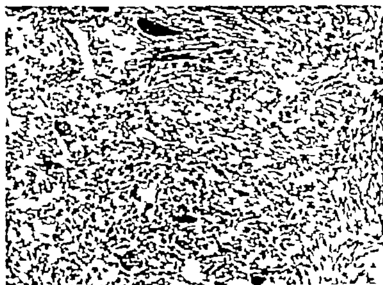


Fig 24-30 Giant cell reparative granuloma of mandible. A few benign giant cells are present but the histologic picture is dominated by fibroblastic cells. Osseous metaplasia, which is almost always present, is seen at the upper left (×100)

Paget's Disease

Paget's disease is of unknown cause. It occurs in middle and old age. The pelvis, femur, skull, tibia and vertebrae are common sites of involvement, although any bone may be affected. In early stages, resorption of bone is prominent. Later there is a mixture of destruction and repair of bone and, in the final stage, the reparative process is predominant and radiopacity is marked. A focal lesion of Paget's disease may simulate primary tumor of bone roentgenologically. With more diffuse involvement of the skeleton differentiation of it from osteoblastic deposits of metastatic carcinoma may be a problem. Widening of the affected bone is helpful evidence that the sclerosing lesion is a manifestation of Paget's disease.

Sarcoma occasionally arises in Paget's disease to complicate the problem of roentgenologic diagnosis. The marked alteration of bone produced by Paget's disease sometimes obscures early signs of a superimposed malignant process.



FIG. 24-31. Paget's disease with characteristic mosaic pattern in irregular osseous trabeculae. Osteoclasts are numerous and the marrow is replaced by vascular fibrous tissue (×50)

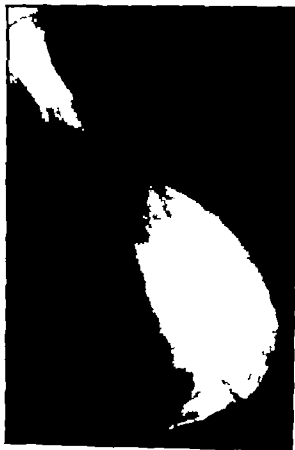


FIG. 24-32. Extreme distortion of humerus by Paget's disease. Such a lesion requires careful biopsy to exclude the presence of sarcoma.

Hyperparathyroidism

Hyperparathyroidism results from neoplasms or diffuse hyperplasia of the parathyroid glands. Ordinarily diffuse demineralization of the skeleton occurs, but marked focal absorption sometimes produces a cystlike appearance on the roentgenogram that can simulate that of a primary neoplasm of bone. In some instances the fibroblastic tissue that fills the defect is so exuberant that the contour of the bone bulges, thereby suggesting even more strongly that a neoplasm is present.

With widespread knowledge of the syndrome of hyperparathyroidism that prevails nowadays, the osseous lesions it produces are rarely subjected to biopsy. The diagnosis is best established by determinations of the serum calcium and phosphorus and by the finding of an increased amount of urinary calcium.

The lesion does not present pathognomonic histologic features. Where the osseous trabeculae are being resorbed, there is proliferating fibroblastic connective tissue usually so richly sprinkled with benign osteoclastlike giant cells that the diagnosis of giant cell tumor may be entertained. The basic fibrogenic quality of the lesion should, however, preclude the diagnosis of giant cell tumor because the latter lesion is not fibrogenic in its proliferating, diagnostic fields.

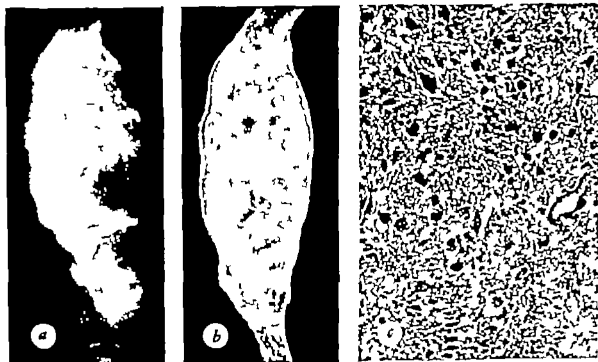


Fig. 24-33 a and b Expanding cystic lesion of hyperparathyroidism involving rib. Note that tumor is composed of fibrous tissue. c Characteristic lesion of this disease. The fibrous tissue contains numerous giant cells of benign type. An almost completely resorbed osseous trabecula is seen at the extreme right (×100)

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